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BUREAU OF HYGIENE AND TROPICAL DISEASES.

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HETEROGENEITY OF STRAINS OF POLYMORPHIC TRYPANOSOMES: ITS RELATION TO NATURAL AND EXPERIMENTAL TRANSMISSION.

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It is probable that every case, or nearly every case, of sleeping sickness is curable by Germanin in the early stage; largely owing to the discovery of this drug, better control of the disease is now possible than formerly. Sleeping sickness is still, however, one of the most important and fatal diseases in tropical Africa as many infected persons are already in an advanced incurable stage when first treated.

Several important and interesting questions require further investigation; the disease varies greatly in clinical severity in different areas, being very acute where the Rhodesian form prevails and comparatively mild, in its early stage, in Gambian sleeping sickness areas. These differences, as is shown by the character of the infections in inoculated laboratory animals, are due to differences in the trypanosomes, some being more virulent than others. Differences in clinical severity are also found in a single area and may be attributed chiefly to differences between "strains" of trypanosomes as well as to differences in individual resistance in the population.

The incidence and significance of inapparent, mild or chronic infections in areas where the disease is mainly acute seem worthy of investigation. The old problem of the relationship of the three so-called species of polymorphic trypanosomes to one another, including the question of reservoirs of human trypanosomes in domestic and wild animals, is an important one which needs further inquiry. A closer examination and analysis of strains of polymorphic trypanosomes than has hitherto been made is required.

Species of Polymorphic Trypanosomes.

The three species of polymorphic trypanosomes are considered by most observers to be indistinguishable from one another morphologically, but they show broad, somewhat ill-defined physiological differences. *Trypanosoma rhodesiense* is only distinguished from *T. brucei* by being known to have infected man; the two human trypanosomes, *T. gambiense* and *T. rhodesiense*, differ in degree rather than in kind in respect of certain qualities—the severity of the infection in man and animals, sensitivity to arsenical and antimonial

compounds, the numbers of posterior-nuclear forms in animals, their geographical distribution, and their principal insect vectors in nature. Both types of human trypanosomes are known to occur in the same territory, though one or the other usually predominates, and strains with intermediate characters have been reported (LESTER, 1933). Whether they should be regarded as forming one species or two is still unsettled but, however they may have originated, it is convenient to speak of them by separate names. It appears to be probable that mixed infections occur—*T. gambiense* and *T. rhodesiense* in man and either of these with *T. brucei* in animals—as there has been ample opportunity during the last thirty years for their introduction into each other's territories. No investigations of this seem to have been made.

Strains.

Laboratory strains of polymorphic trypanosomes are the descendants of samples taken from the blood (usually) of naturally infected persons or animals and their previous history is, of course, unknown, but every strain when isolated, and at least for a considerable time afterwards, must be regarded as being of heterogeneous composition. Although after repeated mechanical transmissions in small laboratory animals an originally polymorphic strain becomes less polymorphic, perhaps through selection with or without adaptive change, the trypanosomes still show physiological differences and, like all populations of living things, except perhaps clones (descendants of single cells), the strain remains to some extent heterogeneous in composition.

All the trypanosomes of a human strain were, of course, able to infect, or at least to live, in the individual from whom the strain was taken ; they were not at that time all necessarily able to infect other persons, and possibly none of them could infect certain very resistant individuals ; in fact, if such a strain of *T. rhodesiense* had been isolated from a naturally infected animal, for example a sheep or an antelope (infected from man by tsetse), and had been tested only on such very resistant persons, it would probably have been called *T. brucei*.

Selection.

The question of what changes may be brought about in collections of living organisms by random sampling and special selection (apart from alterations in protoplasm) is an old subject. That selection must occur during the transmission of polymorphic trypanosomes from one host to another has naturally long been recognized ; it is critically discussed by ROBERTSON (1929) in her paper (*vide infra*) on *Bodo caudatus*. When the sequence of events in cyclical transmission is considered, the importance of selection seems obvious, but it has not been definitely proved and should be investigated.

In the first vertebrate host the composition of the strain must be constantly changing ; the numbers of trypanosomes in the peripheral blood are known to fluctuate at short intervals, and the morphological picture (whatever significance this may have) also changes in respect of the relative proportions of the long and slender, intermediate and short and stumpy forms of a polymorphic strain ; relapse strains with different immunological characters are formed. Hence a single tsetse fly feeding on the same infected animal or man on different occasions would take up different samples of trypanosomes, and two or more flies feeding at the same time would not necessarily take up samples identical in composition.

In the tsetse fly also it is at least very probable that further selective changes in the strain would occur : in the same fly at different feeds, and in different flies, different numbers of trypanosomes, from none to many, would survive

in the gut. Great differences are observed in the proportions of flies infected in experiments with the same strain of trypanosome and the same species of animal and tsetse ; there are no doubt several causes of this but little is known about them. Similarly it is reasonable to think that the composition of a " population " of trypanosomes in the salivary glands of the tsetse fly must vary from time to time in the same fly and in different flies in a single experiment. By a modification of the method used by BRUCE and his colleagues (1913), BURTT (1943) has shown that a tsetse fly ejects, in the act of biting, different numbers of trypanosomes on different occasions ; these quantitative differences may well imply qualitative differences also, such as, for example, varying proportions of trypanosomes of high and low virulence, and, on some occasions no doubt, none sufficiently virulent to produce infection in a host which on another occasion would be infected by the same fly (recorded in man by FAIRBAIRN, 1943).

Finally, the second vertebrate host would exert a selective influence on the strain when the fly bit it, some of the trypanosomes being able to infect it and others unable to do so.

From some experiments it was concluded that the infectivity of a strain depends upon the number of trypanosomes injected—by the syringe (KLIGLER & RABINOWITCH, 1927) or by a tsetse fly (FAIRBAIRN, 1943) ; yet infection has often been produced by the injection of a single trypanosome, and the greater chance of the inclusion of the most infective trypanosomes in the greater number, a qualitative difference, might well explain the results. CORSON (1934) found no appreciable difference between doses of 200 and 100,000 trypanosomes of a virulent strain. The view that mere numbers affect infectivity may be correct but it has not yet been conclusively proved ; the question might be decided by work with clones.

Individual differences among the trypanosomes of a strain are apparent in many laboratory experiments ; trypanocidal drugs and sera, for example, do not kill all the trypanosomes simultaneously and often some trypanosomes survive, as was frequently observed long ago (LEVADITI & MCINTOSH, 1910). Some of the trypanosomes of a strain show greater sensitivity than others to light or ultra-violet rays after treatment with acridine compounds (v. JANCSÓ, 1931, 1932 ; OESTERLIN, 1936 ; HAWKING, 1938); relapse strains may be developed from survivors of the preceding strain.

It is therefore probable that selection plays an important part in the transmission of polymorphic trypanosomes in nature and in experiments.

Protoplasmic Changes.

Apart from the effects of selection, a strain may possibly undergo variation in course of time by actual protoplasmic changes in the trypanosomes ; this has been shown to occur in other protozoa.

WENYON (1926) mentions evidence obtained by JENNINGS and by MIDDLETON proving that " after long periods of multiplication, definite inheritable variations do occur in the descendants of a single individual, and this quite apart from any sexual process. It therefore seems probable that if the observations were continued for a sufficient length of time, it would be possible to separate from the descendants of a single individual, various races which would be as distinct from one another as the naturally occurring races. If this were not so, it would be difficult to understand how evolution could take place at all." The subject is clearly dealt with by JENNINGS (1920) in a published series of lectures.

ROBERTSON concluded from her experiments on the action of acriflavine on cultures of *Bodo caudatus* that changes in the body of the protozoon were

produced, and found also that variation occurred in an untreated clone (the descendants of a single *Bodo*) during two years of culture.

Jollos (1921) exposed clones of *Paramecium* to arsenious acid and found that increased resistance to the chemical developed and persisted during growth in a normal culture medium for several months but it was gradually lost; when the descendants of an isolated conjugating pair were tested it was found that the arsenic resistance had completely disappeared, indicating that the resistance was not a genetic change. In some cases, however, by long exposure to arsenic, a fall in resistance occurred which, since it remained after conjugation, was regarded by Jollos as a genetic change.

The loss by old laboratory strains of polymorphic trypanosomes of their transmissibility by tsetse flies appears to indicate an actual change in the trypanosomes.

Persistence of Changes.

Oehler's (1913) experiments with a strain of *T. brucei* are well known; he made a clone resistant to salvarsan and carried it on by inoculation of single trypanosomes and the subclones were just as resistant as their ancestral clone. He mixed salvarsan-resistant and normal clones of *T. brucei* and inoculated the mixture from mouse to mouse, and was able to distinguish the strains by testing with a solution of salvarsan, the normal trypanosomes being immobilized; after many passages the resistant strain was crowded out by more rapid multiplication of the normal strain. He re-isolated the two strains from the mixed infection by inoculations with single trypanosomes. In these experiments there appears to be no selective process in the development of arsenic resistance.

Clones of trypanosomes were also used by v. Prowazek (1913) and by Broom & Brown (1937, 1938, 1939, 1940) in their study of variation in *T. brucei*.

The loss of the kinetoplast, which may occur spontaneously or be produced by the action of chemicals—oxazine, pyronin and other substances—has been regarded as an inheritable structural change. Werbitzki (1910) found that within 24 hours after the injection of oxazine into a mouse infected with *T. brucei*, 80–90 per cent. of the trypanosomes had no kinetoplast, and in the case of pyronin, 40–60 per cent. The peculiarity was retained through many mechanical passages in animals. Weck (1914) observed "blepharoplastless" [akinetoplastic] forms in the blood of a waterbuck which was naturally infected with a polymorphic trypanosome, while in the case of *T. evansi* also such strains may appear spontaneously in naturally infected hosts (Hoare & Bennett, 1937, 1939). Hoare (1940) concluded that the akinetoplastic condition can be interpreted as a mutation though it also bears some resemblance to cytoplasmic inheritance.

Ehrlich and his pupils (1909, 1911), and other workers more recently, showed that resistance to arsenic can remain unchanged for years in strains of trypanosomes maintained by mechanical passages in animals, while Yorke, Murgatroyd and Hawking (1933) proved that it could remain undiminished after two cyclical passages by tsetse flies. Eagle and Magnuson (1944) reported the apparently spontaneous development of resistance to a group of arsenical compounds by a strain of *T. equiperdum* which had not been exposed to chemicals; they did not think that it was a change produced by selection, but that it resembled more a sudden overgrowth of the parent strain by a variant.

It seems, therefore, that the possibility of the occurrence of heritable change in trypanosomes cannot be excluded, but in a clone spontaneous changes would no doubt be very slow and probably negligible in short experiments.

Sexual Reproduction.

It is the general opinion that trypanosomes have neither conjugation nor sexual multiplication by gametes; the question is critically discussed by WENYON. VANDERPLANK (1944) from observations on *T. rhodesiense*, and FIENNES (1945) from a study of *T. congolense*, concluded that sexual reproduction does take place. If this should be confirmed the subject of variation in trypanosomes would be still more complicated, and the possibility of hybridization between the so-called species of polymorphic trypanosomes, as was suggested by MANWELL (1936) for malarial parasites, would at least need consideration.

Positive and Negative Results.

In transmission experiments with a strain of trypanosomes in which selection plays a part, the retention of a character is a positive result in respect of the individual trypanosomes, while the loss of a character by the strain is a negative result which could be explained as a loss, by the strain, of the trypanosomes possessing the character, through random sampling or selection. The positive result shows what can happen, *e.g.* the retention of infectivity to man after passages in animals, whereas the negative result would not show that any trypanosomes in the strain had lost their ability to infect man as the trypanosomes, infective to the volunteers used, might not have been transmitted, having been "weeded out" by selection; if the experiment were repeated a positive result might be obtained. In some experiments negative results have so little significance that they should be ignored.

Some positive results have been obtained in experiments with strains of polymorphic trypanosomes where cyclical transmission has been used. As mentioned above, YORKE, MURGATROYD and HAWKING found in one experiment that resistance to arsenical compounds was not decreased after two successive passages by tsetse flies. Strains of *T. rhodesiense* (DUKE, 1935; CORSON, 1937, 1939; FAIRBAIRN, 1943) and *T. gambiense* (VAN HOOF, HENRARD and PEEL, 1943) have retained their infectivity to man after repeated cyclical passages through such animals (goats, sheep, pigs, antelopes) as they would be expected to infect in nature. In these experiments the natural mode of transmission from vertebrate host by tsetse fly to vertebrate host was so closely reproduced that there can be no doubt that it occurs in nature, although, so far, none of the attempts to infect man with polymorphic trypanosomes obtained from naturally infected animals have succeeded; there have been few attempts, however, in sleeping sickness areas.

Validity of Conclusions.

Conclusions, and especially generalizations, drawn from the results of experiments in which a strain of trypanosomes has shown changes in its characteristics are open to criticism on the ground of the possible effect of selection. Human strains have been stated to have become less or more virulent, less polymorphic, less or more transmissible by tsetse flies, less or more susceptible to the action of drugs or sera, even to have lost, temporarily at least, their infectivity to man. It was concluded from some experiments, for example, that there were indications that only a certain limited number of individuals of any tsetse population are able to act as hosts for trypanosomes, yet in successive experiments with a certain species of reedbuck, 60, 33, 47 and 52 per cent., respectively, of the tsetse flies which lived long enough to become infective had infected salivary glands. An explanation suggested for such an

exceptional result was that the blood of that species of reedbuck was very suitable for the development of the trypanosomes in tsetse flies; further investigations are desirable.

Only when a considerable number of transmission experiments with considerable numbers of flies and animals have produced uniform results, may it be permissible to conclude that the trypanosomes have changed—have become, say, less virulent; this conclusion would apply to that strain and to the particular experimental conditions such as, perhaps, the species of animal hosts; it might then reasonably be thought to have been due to the influence of the vertebrate hosts and if they were such as would be exposed to infection in nature the result might have some practical importance.

Uniformity of Material in Experiments.

To test the validity of conclusions and especially generalizations, drawn from transmission experiments with strains, it seems to be necessary to try to reduce the variable factors as much as possible. Variation in the vertebrate host could no doubt be much decreased by choosing an inbred strain of mice such as, for example, the *dba* (Little dilute brown) strain (see SNELL, 1942) and using sufficient numbers; a large mouse population would need to be kept and carefully inbred. Variation within a species of tsetse might possibly be somewhat diminished by using pupae from one locality, as different races are known to occur in different areas (BAX, 1944). The use of clones of recently isolated strains of polymorphic trypanosomes would probably greatly reduce variation by eliminating selection. It seems to be the only way of analysing a strain of trypanosomes. Much could be learned, perhaps, about the effect of selection in transmission experiments by using normal and drug-fast clones, separately and in mixtures; arsenic-fast trypanosomes (which are also acriflavine-fast) could perhaps be followed through direct and cyclical transmission, and the same might apply to akinetoplastic trypanosomes in direct transmission; REICHENOW (1940) suggested that the kinetoplast may be essential for development in the tsetse fly. Such "labelled" trypanosomes might be recognizable in various ways—by testing with the drug to which they are fast, by staining, or by measuring their photosensitivity—and might possibly be distinguishable from the "unlabelled" trypanosomes in mixtures, and the varying proportions at different stages of transmission experiments be observed. It would be interesting, for example, to work with mixtures of *T. brucei* and *T. rhodesiense*, one "labelled" and the other not; also to isolate the most virulent clones of strains of *T. brucei* from, say, Zululand, testing them on man. How far technical difficulties or the behaviour of the clones might interfere with the success of such experiments would probably be indicated in preliminary tests.

These suggestions are offered partly because the ease with which tsetse pupae can now be brought to places outside tropical Africa enables such experiments to be made under good conditions in well-equipped laboratories.

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SUMMARY OF RECENT ABSTRACTS.*

III. MALARIA.

Epidemiology.

RENKONEN (p. 621) discusses malaria in Finland, where the only vector is *Anopheles maculipennis* [*typicus* and *messeae*]. Incidence curves show a remarkably consistent peak in May (as in Sweden, North Germany and Holland), and the height of this seems to be affected more by the temperature in April than by that of the preceding September; the explanation favoured is that in a cold April the people remain longer exposed than in a warmer April to the bites of overwintered mosquitoes. The author also thinks that the findings are inconsistent with the view that the spring peak is due to a prolonged incubation period after autumn infection.

PEREPEREZ Y PALAU (p. 171) describes the malaria position of the delta of the Ebro (Spain) where there is considerable cultivation of rice. *Plasmodium vivax* is the commonest parasite. The fact that at certain seasons relatively large numbers of labourers migrate into and out of this region, and may therefore disseminate their infections, makes this a problem of more than local importance.

BUXTON (p. 335) has summarized what is known of the distribution of malaria and anophelines in Arabia; this cannot further be abstracted.

BOURGUIGNON (p. 172) notes that in the Elizabethville region of the Belgian Congo the chief vectors are *A. gambiae*, *A. funestus* and *A. maculipalpis* [the last is not usually regarded as a vector of any importance, and the author does not support his opinion by any detailed facts]. The malaria of this region is almost all due to *P. falciparum*, the local strains of which are very small. He discusses the seasonal incidence of the disease.

GARNHAM (p. 959) reports outbreaks of malaria in a district in the highlands of Kenya (7,500–8,500 feet), where *A. gambiae* (the only vector) and other species of *Anopheles* breed, the former for short periods about May. The mean shade temperature is never high enough for the development of the parasite in the mosquito, but *A. gambiae* spends most of its life in human habitations, where the temperature is 5°–10° higher than outside. The temperature in these huts, about 66°F., is just high enough for the sporogony of *P. falciparum* in May.

BEET (p. 856) states that *P. ovale* infection is quite common in part of N. Rhodesia. JACKSON (p. 244) reports a case of *P. ovale* infection, presumably contracted in New Guinea, where this parasite has not previously been seen.

YACOB and SWAROOP (p. 620) describe the results they have obtained by applying Gill's method of forecasting epidemics of malaria in the plains of

* The information from which this series of summaries has been compiled is given in the abstracts which have appeared in the *Tropical Diseases Bulletin*, 1945, v. 42. References to the abstracts are given under the names of the authors quoted, and the page on which the abstracts are printed.

the Punjab; considerable precision is attained. In comment, WHITE maintains that these predictions have had little value, otherwise they would have been falsified more often by appropriate action.

RUSTOMJEE (p. 684) describes the epidemiology of malaria in Ceylon, where it is common in the dry zone (*P. malariae* being pre-eminent), moderate in the intermediate zone (*P. falciparum* and *P. vivax*), and rare in the wet zone, except for the epidemics which occur from time to time. These epidemics follow deficient rainfall, which leads to drying of the rivers, with the formation of pools in which *A. culicifacies*, the only vector, can breed. *P. malariae* plays no part in the epidemics. D'ABRERA (p. 959) has found that in Ceylon, where during epidemics *P. falciparum* displaces *P. malariae* as the most common parasite, valuable warning of an approaching outbreak may be obtained by charting the ratio between the two in the blood films examined.

PONS (p. 335) has described the physical features of Indo-China in relation to malaria. The chief determining factor is the presence of *A. minimus*, which breeds in the valleys of the mountain areas of the country. He claims that certain races of the inhabitants have adapted themselves to life in the unhealthy valleys, and have developed considerable resistance to malaria; other races have failed to do this.

Although the mortality rate for malaria in the United States was lower in 1943 than ever before, FAUST *et al.* (p. 620) estimate, from extensive blood-film surveys, that there are probably 400,000 infected persons, mostly in the Southern States. They call attention to the possibility of spread as a result of malaria (especially *P. vivax*) in returned soldiers. WATSON and RICE (p. 173) give an account of malaria as it has been observed in North Alabama during a period of 20 years. *P. vivax* is the common parasite, but *P. falciparum* is not rare; the mosquito concerned is *A. quadrimaculatus*.

Aetiology.

WOLPERS (p. 85) has studied the structure, and followed the course of development, of *Plasmodium vivax* by means of the electron microscope. Details should be sought in the original.

It is often assumed that the paroxysms of *P. vivax* malaria have a periodicity of exactly 48 hours, but YOUNG (p. 686) shows that this is not true for some strains; in two strains the periods were 43·4 and 45·7 hours, respectively. The peak of fever coincides closely with the peak of young ring forms in the blood.

SERGIEV and TIBURSKAYA (p. 622) have compared two strains of *P. vivax*, one from northern and one from southern Russia, by infecting two series of paretic subjects. The southern strain showed much lower parasite counts than the northern strain, but more gametocytes and greater ability to infect mosquitoes (probably related to the gametocyte count). There was also some difference in resistance to quinine, but not to mepacrine.

BENNISON and COATNEY (p. 623) have been able to render sporozoites of *P. gallinaceum*, and human blood containing *P. malariae*, non-infective by exposure to X-rays.

RUGE and KREMER (p. 85) observed abnormalities in malaria parasites which appeared in the blood in spite of suppressive mepacrine. These are described, but the details cannot further be abstracted.

Transmission.

GRUNDY (p. 517) has compiled and brought up to date a list of *Anopheles* concerned with transmission of disease in man. References are given to the

authorities for the less well known species, and in all, 99 species are included, almost all of which are implicated in malaria transmission. The other diseases concerned are filariasis and equine encephalitis.

EYLES (p. 435) sums up present knowledge on the range of flight and dispersion habits of mosquitoes. He gives a table of the maximum flight, so far observed, of 20 important vectors of malaria. In comment, MACDONALD makes the point that work on this subject should be extended, since it has so practical a bearing on malaria control. [See also SHAPIRO *et al.*, RUSSELL *et al.*, and HUFFAKER & BACK, below.]

GALVÃO *et al.* (p. 4) discuss the rearing and maintenance of mosquitoes in the laboratory, in a paper which should be consulted in the original.

RAEVSKY (p. 858), after criticizing the methods used for estimating the numerical fluctuations of a mosquito population, describes his own method, which entails a census of all buildings capable of sheltering mosquitoes, and periodical mass collections, or collections in representative sections of the community. He elaborates the uses to which these data can be put.

GEIGY (p. 684) has shown that larvae of *A. claviger* (*bifurcatus*) may survive winter in Switzerland, in frozen ponds and slow streams. He has demonstrated that repeated feeding on a gametocyte carrier results in higher infection rates in mosquitoes than a single feed.

A careful investigation of the anophelines of the Dead Sea area of Palestine by SHAPIRO *et al.* (p. 247) has shown that *A. multicolor* breeds in brackish water puddles (2·5 per cent. NaCl) near the shore, in spite of the nightly rise and daily fall of the water level which causes the disappearance of these puddles during the day. The larvae were found 10–15 cm. below the gravel surface in the daytime. *A. sergenti* breeds in swamps fed by springs, and though breeding is most prolific from spring to autumn, it continues throughout the winter. Strong evidence was found that *A. sergenti* travels from $4\frac{1}{2}$ to 8 kilometres; even the males disperse for long distances, so that their presence does not necessarily indicate the proximity of breeding places. *A. superpictus* and *A. multicolor* breed in the same swamps, but *A. sergenti* is the predominant species.

SHUTE (p. 857) has made counts of the number of sporozoites of *P. falciparum* in the salivary glands of infected *A. maculipennis atroparvus*. The numbers vary greatly, up to 219,450. If the mosquitoes are allowed to feed on a rabbit every two or three days after the estimated time of first infection of the glands, the numbers of sporozoites in the glands are fairly well maintained for 25 days, after which they decline; but there is no uniformity in the discharge of sporozoites.

Little is known of the mosquitoes and of the incidence of malaria in Iran. BEKLEMISHEV and GONTAEVA (p. 248) studied the subject in 1941, in the north-western part of the country. In the uplands *A. superpictus*, *A. maculipennis maculipennis*, *A. sacharovi* and *A. claviger* (*bifurcatus*) are found especially in well-watered country in which standing collections are allowed to form. In the Caspian coastal area, where the climate is sub-tropical, drainage ditches and rice fields are numerous, and *A. maculipennis* and *A. hyrcanus* are found, but in the rivers, where the fish *Gambusia* is present, larvae are not found GUTSEVICH (p. 533) names the anophelines found in northern Iran; *A. sacharovi* and *A. superpictus* are important in relation to malaria, but *A. hyrcanus* is also found.

BIELOGLAZOV (p. 249) reports the wide distribution of *A. maculipennis messeae* throughout the Mongolian People's Republic.

An account of the biology of *A. algeriensis* is contributed by ENIKOLOPOV (p. 859); it is not an effective carrier of malaria, though it feeds on man, its mean duration of life being much less than that of *A. maculipennis*, usually too short for the complete cycle of development of the parasite.

Sautet and Marneffe (p. 336) describe the outdoor resting places of certain anophelines of Lebanon and of the Niger country.

Mattingly (p. 434) has produced new keys to the anophelines of West Africa.

Ribbands (p. 3) has studied the mosquito which was formerly regarded as the *melas* variety of *Anopheles gambiae*, and concludes that the evidence justifies its classification as a separate species, *A. melas*. This mosquito will breed in water of high saline content. Chwatt (p. 860) has studied the morphology and habits of *A. melas* in relation to *A. gambiae*. The morphological differences in the various stages are not, in his opinion, sufficiently clear-cut to permit the classification of *A. melas* as more than a biological race of *A. gambiae*, from which it differs mainly in its ecological preferences and geographical distribution. Ribbands (p. 245) has studied the effect of rainfall, tides and periodic fluctuations on a population of *A. melas* in Sierra Leone. This mosquito breeds in brackish, grassy areas flooded only at high tide and mostly dry in the dry season, and in brackish *Avicennia* mangrove areas. The average size of the adult population is closely determined by rainfall, and peaks occur 20–30 days after the causative rainfall. Increase is also correlated with high tides in the dry season. *A. melas* is present throughout the year, but the population in the wet season is ten times as high as it is in the dry season, and the influence of tides is not so great as that of rain.

Lewis (p. 246) has studied *A. gambiae* around Wadi Halfa, with a view to its control, first as a protection to the town itself, and second for the purpose of creating a barrier which the mosquito (whose breeding is confined to the vicinity of the Nile) cannot pass, so that if it can be eliminated from Egypt north of Wadi Halfa, there would be little risk of its infiltration again from the south. *A. gambiae* breeds in pools among the islands of the cataract, on sandy banks in the river and near its margin; these dry up, and breeding in them ceases, from December to April, but the mosquito reappears in April, probably because it has continuously been breeding in the cataract area. Control by oiling, Paris green and drainage has proved successful, and the larvivorous fish *Gambusia holbrooki* has its uses.

Working in Brazil in 1939, de Oliveira Castro (p. 960) found by experiment that the eggs of *A. gambiae* do not survive long if kept away from water, even in a moist atmosphere. Survival is rather longer at 14°C. than at higher (room) temperature, but even then only 0·1 per cent. of the eggs produced living larvae when they had been kept for 20 days at 14°C. away from water.

By means of the precipitin test, Marneffe *et al.* (p. 247) have found human blood in 55 per cent. of female *A. gambiae* tested in the Middle Niger region.

Wanson and Berteaux (p. 337) have found salivary gland infection in *A. brunnipes* near Léopoldville. It is not a common mosquito, and is therefore not an important carrier.

Covell (p. 623) has contributed a comprehensive paper on the distribution, breeding places, adult habits and relation to malaria of the anophelines of India and the Far East. Of the many species which have been described, 41 are concerned with malaria in these areas, and the paper deals only with these. They are classified as:—12 important vectors, 16 of local importance, and 13 having, probably, no practical importance. During the war the two groups which have been outstanding in relation to malaria are the *fluviatilis-minimus* group in India, Burma and S. China, and the *punctulatus* group (with *moluccensis*) in New Guinea and the S.W. Pacific.

Puri (p. 85) has issued a revised edition of his synoptic tables for the identification of full-grown larvae of the Indian anophelines.

d'Abrera (p. 337) describes the eggs of a number of anophelines of Ceylon; the original should be consulted for details.

Siddons (p. 624) in India has succeeded in infecting 9·4 per cent. of *A. culicifacies* with *P. malariae*, and in transmitting the infection by bite to a healthy subject. He found a much higher infection rate in those mosquitoes which were fed in the period August to February than in those fed in March to July when the weather is hot; in those fed in the colder weather, the gland infection rate was 34·4 per cent. The extrinsic incubation period varied from 22 days at 70°F. to 14 days at 80°F. In the man who was infected by the bite of some of these mosquitoes, parasites were first seen in the blood 30 days after the infecting bite, and the first attack of fever occurred 36 days after infection. Following the account of this work is a paper by the same author (p. 625) in which he shows that the optimum temperature for development and transmission of malaria parasites in *A. culicifacies* is 70°–86°F. provided that humidity is fairly high. Development of *P. falciparum* and *P. vivax* does not take place above 94°F. The extrinsic incubation period for *P. vivax* is 7 days at 86°F.

Russell *et al.* (p. 687) have performed a large experiment on the flight range of *A. culicifacies* in India. The greatest observed distance was between 1·5 and 1·75 miles, in some cases against the wind. The authors have treated their results statistically, and for details the original should be consulted.

Jaswant Singh and Jacob (p. 618) have investigated malaria on the southern coast of the Bombay Presidency. Here the disease is not common on the coastal belt, but is hyperendemic in the foothills and the interior. The distribution coincides with that of *A. fluviatilis*, the only vector, of which, in one place, 11 per cent. were found to be infected; it breeds in slow-running streams. *A. culicifacies* and *A. annularis* were also found, but there was no evidence that in this area they act as carriers of malaria. *P. malariae* is the most prevalent parasite.

In part of Hyderabad State, where an irrigation project has been in existence for some years, the chief vector is *A. fluviatilis*, which here breeds in irrigation canals, rainwater pools and seepages. *A. culicifacies* probably plays a small part in transmission. In this area Abraham and Samuels (p. 619) found *P. malariae* to be the commonest parasite. A control programme which aims at destruction of adult mosquitoes, larval control, and the use of suppressive quinine, has given encouraging results.

Viswanathan *et al.* (p. 625) note that most freshly-fed *A. fluviatilis* leave their places of feeding before dawn, for some outside resting place. This affects the spray-killing of adults as a method of control, and the authors advocate daily spraying where there is no larval control, or spraying twice a week where larval control exists, or on 2 consecutive days, with 2 days' rest, in the period September to November, when the proportion of the mosquitoes which leave the dwellings at night is highest.

A. philippinensis is the only important vector in the deltaic region of Bengal, where the maximum transmission season is from September to November. Iyengar (p. 625) shows that it favours human dwellings as daytime resting places, and that control should include spray-killing. This species breeds in ponds of clean water, and is inhibited by shade. It does not usually breed in rice fields.

Knight and Farner (p. 688) give reasons for thinking that *Anopheles punctulatus moluccensis* should be known as *A. p. farauti*.

Reeves (p. 437) has carried out precipitin tests on blood from the stomachs of freshly engorged American anophelines of various species.

Hess and Hall (p. 626) note that *A. quadrimaculatus* breeds only in waters on which there is abundance of vegetation or floating material, and have classified the plants which are important in malaria control, from this point of view, in the area concerned. Schoof *et al.* (p. 626) have shown that larvae

and pupae of *A. quadrimaculatus* and *A. punctipennis* can survive for some days in mud, but the precise length of time is not known. Burgess and Young (p. 437) give the results of their investigations into the handling and feeding of *A. quadrimaculatus*. For details the original should be consulted. Huffaker and Back (p. 687) have found that *A. quadrimaculatus* does not usually move in significant numbers more than one mile from its breeding place, but exceptional circumstances may permit it to do so. A very few individuals may travel 3 miles.

In the Annual Report issued jointly by the Government of Trinidad and the Rockefeller Foundation (p. 617) the point is made that *A. aquasalis* is an important vector, but that it is strongly zoophilic in habit. It seems that the presence of buffalo stables near a village has a strong effect in keeping down the incidence of malaria in the inhabitants, and it is suggested that traps baited with animals may be used in malaria prevention. In the wetter parts of Trinidad, transmission is effected by *A. bellator*, which breeds in the bromeliads which are parasitic on the shade trees of cocoa plantations. Suggestions are made, and experiments have been carried out, on the removal or destruction of these plants.

Cochrane (p. 86) has produced circumstantial evidence of some weight that *A. argyritarsis* may be a vector of malaria in Grenada.

Bevier (p. 614) states that *A. darlingi* is the only known vector of malaria in the coastal belt of British Guiana, and that in 1943 it accounted for 96 per cent. of all anopheline captures. It almost completely disappeared in the drought years of 1938–41, but reappeared with the heavy rains of 1942–43. It does not seek acid or brackish waters. With the increase in the abundance of this mosquito there was a corresponding increase in the amount of malaria, for which *P. falciparum* was largely responsible, though *P. vivax* and, to a smaller extent, *P. malariae*, were found. Giglioli (p. 615) also states that *A. darlingi* is the only vector in Georgetown, British Guiana, where it breeds extensively in the suburbs. It disappeared during the drought, but its re-appearance after the rains caused an epidemic of malaria. *A. darlingi* breeds in the drainage system of a cemetery and in rice grounds and cane fields; its eggs die in water containing more than 0·6 per cent. of NaCl. Where malaria is abundant, *P. falciparum* and *P. vivax* are common, but during the drought, when malaria was rare, most of the infections were due to *P. malariae*, rarely seen in times of epidemics.

Unti (p. 86) has studied the viability of eggs of certain anophelines of Brazil, when kept in moist earth.

Larvae of certain S. American anophelines die when the dissolved oxygen content of the water is reduced to 1·5 p.p.m. Unti (p. 86) concludes that pollution of water with organic matter, by decreasing the oxygen content, may be an efficient and economical anti-larval measure. The same author (p. 87) has failed to find any correlation between the iron content of water and anopheline breeding.

Transfusion Malaria.

McClure and Lam (p. 627) report two cases of transmission of *P. malariae* by the transfusion of blood which had been refrigerated for 5 days. The two donors were Sicilians who had lived for 30 years in the United States, and who, presumably, had not been infected there.

Officer (p. 688) has shown by experiment in man that the routine course of anti-malaria treatment, given to a recipient immediately after transfusion of malarial blood, prevents the disease. In cases of emergency, therefore, a potentially malarial donor may be used for transfusion.

Stohlmann (p. 174) reports the transmission of *P. vivax* from an infected patient to three donors of blood transfused directly to him, without storage. There must have been some reflux of blood through the apparatus used. In comment Mollison points out that direct transfusion is now very rarely used, but adds that transmission from donor to recipient is possible even when the blood has been stored for some days.

Tests.

Soberón y Parra (p. 174) describes an intradermal test for malaria in which the antigen is prepared from the blood of a fowl heavily infected with *P. gallinaceum*. The results indicate a large measure of specificity.

Heidelberger and Mayer (p. 689) have found that an antigen prepared from normal human red blood cells is as effective as (and more readily available than) the antigen prepared from *P. gallinaceum*, in the complement-fixation test for malaria. By this test 28 per cent. of sera from malarial patients were positive.

Bogen (p. 861) describes a test which depends on the fact that serum in malaria is precipitated by a stock buffer solution diluted with four times its volume of distilled water. This test is strongly positive during and for some time after an attack; it may be useful in diagnosis or for epidemiological investigations, and in prognosis.

Wood (p. 250) has found that the red cell sedimentation test provides a useful means of differentiation between malaria (in which the rate is high) and infective hepatitis (in which it is relatively low), in their early stages.

Rosenberg (p. 440) has investigated six serological tests for syphilis, to determine their relation to malaria. He concludes that, of all the generally accepted tests, the Hinton test gives the smallest percentage of false positive reactions in malaria; that malaria can often be distinguished from syphilis by the pattern of positivity of tests; and that persistence of positive reactions beyond 6 weeks, in the absence of continued malarial infection, should arouse suspicion of syphilis. Potter *et al.* (p. 690) tested 100 men, suffering from malaria (99 *P. vivax*) with the Wassermann and Kahn tests. All had previously given negative results, and were presumably free from syphilis, but 12 were now positive and 10 doubtful. The results all became negative within 30 days [the patients, presumably, having received anti-malaria treatment].

The sera of a high proportion of patients with malaria were found by Coleman (p. 250) to contain the Vi agglutinins of *Bact. typhosum* in high titre. This may be because the parasite possesses a Vi antigen, or the reaction may be anamnestic.

Shepherd (p. 4) has devised a radiological technique for demonstrating the spleen without the use of any contrast medium. Measurement of the size of the spleen can thus be made, and the method may be useful in relation to malaria.

Pathology.

Rigdon (p. 689) has found evidence that infarcts of the spleen in *P. falciparum* infection may result from obstruction produced by hyperplasia of cells in the walls of the venous sinuses, to which leucocytes and red cells may adhere.

Marshall (p. 438) reports a case of spontaneous rupture of a malarial spleen, without any history of trauma.

Attention is drawn by Kern and Norris (p. 341) to the fact that the liver becomes enlarged, and shows other (biochemical) signs of involvement in half of the patients with malaria. This may occur in a first attack, and is not a sign of chronicity.

Dähne (p. 338) has found that reticulocytosis occurs in malaria patients who are anaemic, about one week after treatment has been started. The blood sedimentation rate is high in such patients, but not in patients who are not anaemic.

Clinical Findings.

Hunt (p. 5) relates his experience of malaria in West Africa and in North Africa. In the latter, subtertian infection was much more alarming and demanded intravenous quinine therapy much more often than in West Africa. He emphasizes the fact, which is so often forgotten, and re-learned at a cost, that subtertian malaria is a dangerous disease which mimics other conditions, to the confusion of the unwary. It should never be lightly regarded.

Ferriman (p. 438) writes of his experience in West Africa of 2,000 cases of malaria in white R.A.F. men, most of whom had never before been exposed to the disease. Almost all the infections were due to *P. falciparum*, but pernicious attacks were not common, suppressive mepacrine (0·2 gm. twice a week) being enforced. Positive blood slides were not found in all cases, and the author comments on the value of splenomegaly as an aid in diagnosis. "Sub-clinical malaria" was not uncommon, the chief symptom being recurrent headache; this was relieved by anti-malaria treatment.

Hyman (p. 962) gives a list of mistaken diagnoses made in 100 men whose illness was subsequently found to be malaria, during the early days of the campaign in the Solomon Islands. These were chiefly diagnoses of cardiac, pulmonary and abdominal conditions, but arthritis, diseases of the brain or other parts of the head, kidney, thyroid and scrotum, were also diagnosed. Later, an outbreak of dengue added to the difficulty of diagnosis.

Gayid (p. 5) notes that in the Middle East, *P. vivax* infections were frequently atypical. He gives details of the standard quinine-mepacrine-pamaquin treatment adopted in that area.

In the province of Voronezh, Russia, which at one time in the war was under German domination, Steinberg *et al.* (p. 339) have found that malaria in children frequently runs an unusual course, regardless of the species of parasite, which may cause it to be mistaken for other diseases. This may be due to importation of new strains, or to alteration in virulence as a result of serial passage through undernourished human hosts. Kassirsky (p. 628) refers to the fulminating type of *P. vivax* infection which has previously been described in Russia.

Boyd (p. 175) has studied the parasite density in persons with naturally induced *P. vivax* malaria, at different stages of the infection. Great variation was observed, for details of which the original abstract should be consulted.

Gordon *et al.* (p. 692) describe the clinical features of relapsing *P. vivax* malaria in soldiers evacuated from the South Pacific. The strains showed a pronounced tendency to relapse, but the attacks were relatively mild and were easily controlled by mepacrine. In rehabilitation the development of physical fitness and the restoration of self-confidence were important.

Boyd and Kitchen (p. 174) give details of their observations on the renewal of clinical activity in naturally induced *P. vivax* malaria, both after spontaneous remission and after remission due to administration of drugs. The facts presented are so numerous that further condensation is not possible.

From an experience of the course of malaria in British troops who escaped from Italy into Switzerland, Anderson *et al.* (p. 961) conclude that the influence of a high altitude climate (Adelboden, 4,300 feet) is very beneficial in the relapsing benign tertian type.

McGinn and Carmody (p. 341) describe 16 patients with cerebral malaria, all ascribed to *P. vivax*. Fitz-Hugh *et al.* (p. 340) describe cases of cerebral

malaria among troops stationed in India, noting several cases in which the infection was due to *P. vivax* or *P. malariae*, though the majority were due to *P. falciparum*. In a well-nourished group, previously in a high state of physical fitness, the death rate was much lower than in another group of lower standard, though the incidence did not greatly differ. The association of convulsions and coma carried a grave prognosis, especially if the parasite count was high ; on the other hand, in some fatal cases there were few demonstrable parasites. Viswanathan (p. 691) discusses the pathogenesis of cerebral malaria, and describes several fatal cases in which a well-formed ante-mortem clot was found in the sagittal sinus. This, he thinks, has not previously been reported.

Das Gupta and Ganguli (p. 338) describe a fatal case of *P. falciparum* infection in which large numbers of gametocytes in all stages of development, and of schizonts, were present in the peripheral blood.

In Panama, Applebaum and Shrager (p. 176) have investigated 125 cases of pneumonia associated with malaria, chiefly in young white men. The pulmonary lesions were most commonly lobular in distribution ; the combination was not severe ; in one group the condition yielded to sulphonamide treatment, but in another it yielded to anti-malaria treatment alone. In most of the sputa examined no pathogenic organisms could be found.

Robertson (p. 439) writes on lesions of the eye in relation to malaria. The most common is ulcer of the cornea, often with recurrent iritis, but optic neuritis and amblyopia have also been found.

Merrill (p. 691) has observed patients in the United States forces, who, having had malaria, complain of chills which they attribute to malaria but which are not accompanied by fever, and which are of psychogenic origin. Arbuse (p. 963) makes the point that although neuropsychiatric symptoms may occur in malaria, they are usually consistent with the personality of the patient, and are activated by that disease, as they may be by other organic diseases.

Harvey (p. 963) describes a type of peripheral neuritis associated with *P. vivax* malaria, which was quite common in one large American military hospital.

Harrison and Dakin (p. 176) report a case of nephrosis, associated with *P. malariae* infection, in the south-west Pacific ; it is not certain that the malaria was responsible for the condition, but it is not unlikely.

Manson-Bahr and Muggleton (p. 434) record a case of unusually long persistence of *P. ovale* infection.

Kean and Smith (p. 338) note that if the inhabitants of Panama survive childhood, they are unlikely to die of malaria ; the number of parasites in the peripheral blood is not a good index of the severity of the case.

Charles Wilcocks.

[*To be continued.*]

RABIES.

A Review of Recent Articles. XLIV*

(i) *Virus.*

Bailly[1] points out that there is scarcely any "organic liquid, humour, secretion, excretion or parenchymatous pulp" of which the action on the virus of rabies has not been investigated but, curiously enough, as far as he

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* For the forty-third of this series see this *Bulletin*, 1945, v. 42, p. 674.

[1] Bailly, J. Action de l'extrait de pancréas sur le virus de la rage. *Bull. Acad. Méd.* 1945, v. 129, Nos. 13, 14 & 15, 255–7.

could determine, no one had thought of studying the action of pancreatic juice. The author points out (and he has apparently been considering mainly the possibility of proteolytic action) that if he had been able, at the time he thought of carrying out his investigations, to procure some of Northrop's crystallized preparation of trypsin he would have used that. He decided to use a watery extract of pancreas from a dog and he outlines his method of preparation, which was carried out at low temperature. After the extraction had proceeded for a period of 48 hours he tested the amylolytic effect of the maceration on starch, and since such activity was demonstrated, he believed he was justified in his surely hazardous assumption that it would possess proteolytic activity. His virus suspension consisted of a 1 : 50 suspension of the brain of a rabbit inoculated with a fixed strain of virus. This suspension had been filtered through filter paper to remove the larger particles of tissue. The author states that a number of experiments were performed along similar lines and he has recorded the results of some of these as being typical. Two sets of tubes were put up in each experiment, one containing the virus suspension and equal parts of the pancreatic extract and the other the virus suspension with equal parts of physiological saline. The alkalinity of the mixtures was adjusted (somewhat crudely ?) by the addition of sodium carbonate, but he does not state clearly what indicator he used ; the recorded pH values of the mixtures ranged between 10 and 12 and were stated to be similar in the control tubes. The mixtures were kept at 10°C. for 24 hours. The results of two experiments are recorded ; in one, 4 mice were inoculated with the mixture of virus with pancreatic extract and 2 with the virus in saline, and in the other 5 guineapigs were inoculated with the pancreatic-extract-virus mixtures and 2 guineapigs with the control mixture without pancreatic extract. The 4 mice and 5 guineapigs inoculated with the virus-pancreatic-extract mixtures survived, and the 2 mice and 2 guineapigs inoculated with virus alone, died of rabies. The author concludes that the " rabic virulence " of brain suspension was destroyed by the aqueous extract of pancreas of a dog in 24 hours at 10°C. He also made some experiments in which he states that the recorded pH values of the several mixtures of virus with or without pancreatic extract ranged between 6 and 8·4 (in one of these experiments a " street " strain of virus was employed instead of a " fixed " strain and in the other the strain is not stated). In these tests also, only a limited number of animals were inoculated with the mixtures, a total of two rabbits and four guineapigs with the mixtures of pancreatic extract and virus and one rabbit and two guineapigs with the virus mixtures and all the animals died of rabies. The author concludes from a consideration of all the results that, since the destructive action of the pancreatic extract on the virus of rabies was dependent on the alkaline reaction of the medium, this shows that it was due to the activity of trypsin, and that the destructive action on the virus was proteolytic in nature. [Some of the details of these experiments have been stressed because it is felt that it would be unfortunate and misleading if they were subsequently referred to as conclusive evidence of the destructive action of a pancreatic extract (or trypsin) on the virus of rabies. Surely it would be necessary to make such studies on a quantitative basis, especially as regards the relative virus content of the original suspensions (a gradocol filtrate would be preferable) and the control mixtures without pancreatic extract, at such a high alkalinity as pH 11 or 12. The stability of the virus in media of different pH values should form the subject of a preliminary investigation. It might quite well be that the amount of virus surviving in certain hydrogen-ion concentrations is low, and if few test animals are inoculated the probability of detecting virus would be a question of chance. The optimum pH value for tryptic activity is less alkaline than pH 11 to 12 and although trypsin would be to a certain extent protected by

protein in the substrate, one would expect the activity of trypsin to be much reduced above *p*H values of 8–9.]

Kanazawa [this *Bulletin*, 1937, v. 34, 671], Webster and Clow [*ibid.* and 1938, v. 35, 168], Bernkopf and Kligler [*ibid.*, 1938, v. 35, 641, and 1941, v. 38, 494], and Schultz and Williams [*ibid.*, 1938, v. 35, 641] reported the successful cultivation of "fixed" strains of rabies virus in relatively simple media consisting of fragments of rabbit, mouse, rat or chick embryo brains in Tyrode's solution. Whereas Kanazawa did not add serum to his medium, Webster and Clow incorporated 10 per cent. monkey serum, and Bernkopf and Kligler recorded that they found the addition of human or monkey serum, but not rabbit serum, to be favourable to the multiplication of the virus. Subsequently Webster [this *Bulletin*, 1938, v. 35, 646], Kligler and Bernkopf [*ibid.*, 1939, v. 36, 728] and Hodes, Webster and Lavin [*ibid.*, 1941, v. 38, 161] reported on the antigenic value and potency of vaccines prepared from such tissue cultures. The virus potency of the tissue cultures appeared to be somewhat lower than that of fresh brain material from mice or dogs infected intracerebrally with "fixed" rabies virus. The last-named authors therefore attempted to increase the virus content of the tissue cultures by several methods, without success, but they obtained a 10-fold concentration of the culture virus by freezing and drying. Webster and Casals [this *Bulletin*, 1942, v. 39, 82] stated later "that from a practical point of view culture virus had not proved a satisfactory source of rabies vaccine due chiefly to its low virus content."

In later experiments on the vaccination of mice and dogs Webster and Casals [this *Bulletin*, 1941, v. 38, 496, and 1943, v. 40, 201] reverted to fresh brain material from mice and dogs infected intracerebrally with "fixed" rabies virus as a source of antigen for vaccine production. [It is interesting to note that Plotz and Reagan [this *Bulletin*, 1942, v. 39, 589] reported the successful cultivation of "street" strains of virus in culture media consisting of chick-embryo brain tissue in Tyrode's solution with monkey serum and chicken plasma.]

Parker and Hollender[2] now bring confirmation of the possibility of propagating "fixed" strains of rabies virus in tissue cultures similar to those used by the earlier workers. They have extended the observations of the latter and have recorded a number of interesting findings. They used different strains of "fixed" virus that had been passaged for various periods in mice. The "Squibb" strain had been passaged 12 times in mice, the "Webster" strain 126 times, and the "Alabama" strain 109 times. The "Alabama" strain "gave the best results" in that the cultures appeared to have a higher virus potency, but as the technique was modified in the later experiments, which were made with the "Alabama" strain only, it would be difficult to associate these results with any special attribute of this particular strain. Finely chopped embryo mouse brain was used as the tissue component of the medium, one large brain or its equivalent being used for each culture. In the early experiments the fluid phase of the culture consisted of heated rabbit serum (1 hour at 56°C.) (constituting $\frac{1}{4}$ or $\frac{1}{3}$ of the final mixture) or of ox serum ultrafiltrate ($\frac{1}{3}$) (see Simms and Sanders, *Arch. Pathology*, 1942, v. 33, 619), together with 1·4 per cent. sodium bicarbonate ($\frac{1}{6}$), and Tyrode's solution containing four times the usual amount of glucose. The *p*H of the mixtures was adjusted to 7·2, "by means of a gas mixture" before the tissue was added, and thereafter the cultures were "gassed" with a mixture of

[2] Parker, R. C. & Hollender, Augusta J. Propagation of Rabies Virus in Tissue Culture. *Proc. Soc. Exper. Biol. & Med.* 1945, Oct., v. 60, No. 1, 94–8. [Refs. in footnotes.]

oxygen (21 or 80 per cent.), carbon dioxide (8 per cent.), and nitrogen. In the later experiments the fluid medium consisted either of heated rabbit serum or ox serum ultrafiltrate ($\frac{1}{3}$) combined with Simms's X7 solution (see SIMMS and SANDERS *loc. cit.*). As an indicator of *p*H all cultures contained either 0·001 per cent. or 0·005 per cent. phenol red. Another feature of the later experiments was that the culture tissues were ground when passages were made. It had been found by comparative inoculation tests, in mice, for virus potency, with ground and unground tissues, that grinding is necessary in order to liberate the main bulk of the virus from the tissues. There was little to choose between the two methods of grinding, with quartz sand or with Tenbroeck grinders. In all the later experiments 125 cc. Erlenmeyer flasks were used, whereas in the earlier experiments Carrel flasks with only 3 or 4 cc. of medium were used.

Comparative tests with cultures containing heated rabbit serum or, on the other hand, ox serum ultrafiltrate showed, that beyond the sixth passage, in which passage the rabbit serum cultures had a higher titre than the ox serum ultrafiltrate cultures, it was not possible to detect any appreciable difference between the two sets of cultures. A duplicate series of cultures incubated for nine passages at 35°C. and 37°C., respectively, showed no consistent difference in the amount of virus produced.

Comparative tests showed also that the subjection of the cultures to continuous " gassing " with the mixtures of O_2, CO_2, and N_2 had no real advantage " provided that the buffering system in the medium is capable of maintaining the *p*H value at an optimum level " [this optimal level is not stated]. The results of other experiments showed that embryo mouse brain culture virus could be maintained in cultures prepared from the brains of 5-day-old mice, the brains of 14-day-old mice were less satisfactory and the brains of 28-day-old mice [48-day-old mice in the summary] were quite unsuitable. [No mention is made of any attempt to propagate virus recovered directly from the brains of infected mice in cultures with 5-day-old brains.] Unsuccessful attempts to propagate the rabies virus in chick embryo brain cultures are recorded. The source of the virus in these experiments was either virus passaged in mice or in mouse embryo brain cultures, or mouse virus adapted to chick tissue by several intracerebral passages in chick embryos in eggs. In all experiments two passages of 3 and 4 days, respectively, were made each week.

In early experiments with the " Squibb " strain, the virus was successfully passaged 57 times during a period of 28½ weeks ; at the 41st passage mice were infected with a 10^{-5} dilution of the culture tissue, but by the end of the experiment the limiting infective dilution had fallen to 10^{-2}.

Three experiments, two of seven passages and one of eight, were made with the " Webster " strain of virus, but at the end of the experiments the limiting infective dilution of the cultures was not higher than 10^{-4}. In one of the later experiments, with the " Alabama " strain, with which " the most satisfactory results " were obtained, 19 passages were made and in the protocol of the experiment it is stated that " at the 19th transfer (passage) the culture virus killed mice at a dilution of 10^{-6}," whereas in the summary and conclusions the authors report that " the virus multiplied to the extent that mice were killed regularly by the culture material in dilutions as high as 10^{-6}." It is not clear whether this represented the limiting infective dilution of any culture of the series or whether some culture passages had somewhat lower virus titres. In the early passages in mouse embryo brain cultures of another series with the " Alabama " strain, limiting infective dilutions (see Table I) of 10^{-4} to 10^{-5} are recorded. It would be interesting to know also what the virus titres of subsequent culture passages (if any have been made) prove to be. (The virus titres of the cultures in the experiments with the " Squibb " strain

appeared to be relatively good up to the 41st passage but later deteriorated very much.)

In the experiments with the "Alabâma" strain the limiting infective dilution of the original virus in mouse brain was not determined, but all four mice inoculated with a 10^{-7} dilution contracted rabies.

(ii) *Symptomatology and Diagnosis.*

RIFKIN *et al.*[3] record that rabies had never been known to exist on a certain large island in the Pacific which came to be used during the war as a base, with an important harbour and greatly increased shipping. Dogs were introduced from the mainland and at first it was thought that rabies had been brought in also. This suspicion arose when two dogs which had been kept as pets suddenly became excitable and vicious, had epileptic fits and also bit six marines. Inclusion bodies which were considered at first to be similar to Negri bodies were found in sections of the brains of these dogs, but no animal inoculation tests were made. A course of Pasteur vaccination treatment was therefore given to the marines. Later a limited number of guineapigs, rabbits and mice were inoculated with brain suspensions of dogs showing similar nervous symptoms, but no rabies developed in these test animals. The incidence of dog distemper on the island was very high and the clinical pictures of the nervous cases were "identical" with those recorded in rabies. A veterinary surgeon who was a member of the team brought four cases of nervous distemper for investigation, and inclusion bodies similar to, but not characteristic of, Negri bodies of rabies were found in sections of their brains, trachea, bronchi and bladders; inoculation of guineapig, mouse and rabbit with suspensions of brain gave negative results. The inclusion bodies could be found in the ganglion cells of the cerebrum, mid-brain, medulla and in the Purkinje cells of the cerebellum. They were found in sections of the medulla and *Cornu Ammonis* of the first two dogs referred to above. They were about 2–10μ diameter, oval in shape, stained red with Mann's stain and in certain cases had a vacuolated structure but without internal granulations as seen in rabies. The authors cite a reference in 1943 to the occurrence of such inclusion bodies in the brain and other organs of dogs infected with distemper, and point out that their occurrence might lead to a mistaken diagnosis of rabies, if animal inoculation tests are not made also. [The inclusion bodies under discussion, which are associated with cases of nervous distemper in dogs, are commonly known as Lentz bodies. They were first described by that author in 1907 (*Cent. f. Bakt.*, 1. Abt. Orig., v. 44, 374). Descriptions of these bodies are found also in papers by BABÈS and STAROVICI, 1912 (in *C. R. Soc. Biol.*, v. 73, 229), SINIGAGLIA, 1913 (*Pathologica*, v. 5, 107), and KANTOROWICZ and LEWY, 1922 (in *Arch. wiss. prakt. Tierhlk.*, v. 49, 137) and others. GREEN and EVANS, 1939 (in *Cornell. Vet.*, v. 29, 35) recorded their occurrence in the tissues of foxes, mink and ferrets infected with distemper.]

RODRIGUEZ[4] has compared results obtained in diagnosing rabies by histopathological methods with those secured by inoculating groups of five mice with suspenions of brain tissue from the suspected cases of rabies. The former methods included examination of smears and sections for Negri bodies and examination of sections of different parts of the central nervous system, including the medulla, the *ganglion nodosum* of the vagus, and sympathetic

[3] RIFKIN, H., CEKADA, E. B., ZARROW, M., HENDERSON, D. G. & WHITEHEAD, J. O. The Diagnostic Significance of Inclusion Bodies in Rabies and Canine Distemper. *J. Lab. & Clin. Med.* 1945, Sept., v. 30, No. 9, 748–51.

[4] RODRIGUEZ H., H. Sobre el diagnóstico histopatológico de la rabia. *Bol. Inst. Bact. Chile.* 1943, Oct., v. 2, No. 3, 111–20, 3 figs. [23 refs.]

ganglia such as the stellate ganglion, for the several infiltrative and degenerative lesions originally described by BABÈS (*Ann. Inst. Pasteur*, 1892, v. 6, 209, and *C. R. Soc. Biol.*, 1908, v. 64, 284), GOLGI (*Berlin Klin. Woch.*, 1894, v. 31, 325), RAMON CAJAL and DALMACCO GARCIA (*Bull. Inst. Pasteur*, 1905, v. 3, 298) and, in nerve ganglia, by VAN GEHUCHTEN & NELIS (*Ann. Med. Vet.*, 1900, v. 49, 243).

In all, 200 cases were examined comparatively and it was reported to the author that rabies virus had been demonstrated by the inoculation of mice in 119 of these; no virus was demonstrated in 81 instances. By the combined examination for Negri bodies in smears and sections and for the infiltrative and degenerative lesions, rabies was diagnosed in 115 of the cases and negative results were recorded in four, *i.e.* a percentage error, judging by the mouse tests, of 3 per cent. The percentage errors recorded were, when the diagnosis was made by examination of smears alone for Negri bodies, 27 per cent.; by examination of sections for Negri bodies, 20 per cent.; and by the combined examination of sections and smears for Negri bodies, 15 per cent. The infiltrative and degenerative lesions were intense in 79 per cent. of cases and moderate in 21 per cent. Forty-eight of the cases reported to be negative by the histopathological methods were definitely so, and this was a percentage of 59 per cent. of the 81 cases reported to be negative in the mouse tests. Thirty-seven were recorded as doubtful, and four of these were diagnosed as rabies by inoculation of mice.

(iii) *Pathology.*

NEUJEAN[5] reports that during the last three years he had to examine numerous dogs to determine whether they were infected with rabies. The procedure adopted, which was considered very satisfactory, was to inoculate suspensions of the brain into rabbits and mice and to examine sections for Negri bodies. He had been struck by the "polymorphism" of these bodies and the irregularity of their distribution. In addition the author noted the existence of small forms "like dust" dispersed outside the nerve cells, among the nerve fibres, and in certain cases "ramified filamentous forms resembling a mycelium," which were difficult of interpretation.

He had been impressed by a suggestion of BRUMPT in 1938 in relation to the possible re-classification of the viruses of vaccinia and rabies, which he now regards as prophetic. In view of these preliminary observations he tried culture methods which had been successful for growing rickettsia, and he claims to have demonstrated the presence of the "parasite of rabies" by haemoculture. He describes the technique as being surprisingly simple. The blood from animals infected with rabies was collected in the presence of liquoide (Roche) [liquoide is described in the literature as a preparation of sodium polyanethol sulphonate, for use in culture media to prevent coagulation and to abolish the bactericidal power of the blood]. In the beginning this blood was sown into two media, Tyrode and Tyrode with 1 : 1000 agar. The examination of these media which had been sown with the blood suggested "suspicious images" only. However, on examining the "blood-liquoide" which remained after the sowing of the media he found an "intense multiplication of corpuscles presenting all the characteristics, morphology, tinctorial affinity and structure, of the corpuscles met with in rabies, from anhistic bodies to noticeably vacuolated corpuscles and bodies usually called Negri bodies—from the limit of visibility to giant forms." Such "multiplication" was detected when the blood-liquoide had been kept at about 25°C. for 3 to 4 hours. Examination of the blood was carried out by taking a loopful and

[5] NEUJEAN, G. Mise en évidence par hémoculture du parasite de la rage. *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 139–41.

making smears, which were stained by the May-Grünwald-Giemsa method or by Lestoquard's method. The author states that the use of heparin or sodium citrate as anticoagulants appeared to hinder multiplication of the "parasite", which was found only with difficulty and showed "profound morphological changes."

Positive haemocultures were recorded with blood samples collected in advanced stages of the disease from four rabbits infected with the Pasteur "fixed" strain of virus, and from one rabbit and one dog inoculated with a "street" strain of virus. No attempt appears to have been made by the author to correlate the presence of the "parasite" with the infectivity of the blood for susceptible animals by intracerebral inoculation. He intends, however, to secure further information on the time of the appearance of the "corpuscles" in the blood in relation to the course of the disease, and more convincing evidence may be forthcoming. [Confirmation of these observations is necessary. At this stage it is difficult to comment on what has not yet even reached the stage of being *sub judice*. The results reported would seem to be at variance with the irregular results reported in the literature in attempts to demonstrate the presence of the virus of rabies in the circulating blood, but the methods employed up to the present may have been inadequate.]

(iv) *Methods of Treatment and Statistics.*

Ceccaldi[6] reports that two "fixed" virus strains are maintained by rabbit passage at Brazzaville. One is the Pasteur strain, which was passaged 21 times during 1943, and the other is the strain "jeune chien" of Brazzaville, which was also passaged 21 times in 1943, and was in its 244th passage. Recently, for the production of vaccine, the Pasteur strain has been inoculated into sheep. This was necessitated by the shortage of rabbits and the need to produce relatively large quantities of vaccine. [A similar procedure has been forced on a number of other Institutes during the war period.] The virus is maintained entirely in rabbits; the sheep are inoculated for vaccine production only four times during the year. The vaccine up to November 1943 was prepared by the Semple method from 1 per cent. cerebral tissue with 0·05 per cent. carbolic acid, and was then changed so that the concentration of brain was 5 per cent. and of carbolic acid 1 per cent. The vaccine is considered to "maintain its efficacy" for a period of three months if kept in the cold. The opinion now held is that the rabies virus which occurs in French Equatorial Africa is "normal" in virulence, and that bitten people should be treated by the same methods as those applied in Western Europe and other parts of Africa. Ten strains of "street" virus were recovered during the year, eight from biting dogs, one from a horse, and one from a human being who died 21 days after the commencement of treatment 24 hours after a severe bite in the deltoid region. Negri bodies were demonstrated in the brain of the human patient and a "street" strain of virus was recovered. The case of the horse is described in detail but no history of a bite is given. Negri bodies were found in the horse's brain, but they appeared to be infrequent and were small in size.

The chief interest in the report for 1943 by Durieux[7] of the activities of the Pasteur Institute in French West Africa is to be found in the observations on the results of vaccination of human beings against rabies since decentralization of the service was instituted in 1937. During the years 1938 to 1942, 1,122 patients were treated and four deaths occurred before the end of the

[6] Brazzaville [A.E.F.]: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1943 [Ceccaldi, J., Director]. 21–32. Rage.

[7] Afrique Occidentale Française: Rapport sur le Fonctionnement Technique de l'Institut Pasteur en 1943 [Durieux, C.]. pp. 43–53. Service de la rage.

vaccine treatment. The decentralization would appear to be especially advantageous in cases of severe bites. Previously, treatment was not commenced in some instances until 12 days after the bite. On the other hand decentralization, when carried too far, might have disadvantages. In outlying districts it is considered better to transport the patient to the centre where the vaccine is kept, than to await the arrival of the vaccine, which might lose activity in transit. The opinion is expressed that the dose of vaccine for children should be the same as for adults unless they are nurslings, for whom it could be reduced slightly.

(v) *Neuroparalytic accidents.*

KOENIGSFELD[8] reports that a patient aged 43 years was bitten by a dog on 1st January, 1944. Anti-rabies vaccine treatment was commenced at once and 10 cc. of vaccine was given over a period of 14 days. The vaccine, prepared according to Semple's method, consisted of a 5 per cent. suspension of the brain of sheep infected with the Pasteur (Paris) strain of "fixed" virus. During the period of vaccination, and contrary to advice, the patient consumed alcohol, but only in moderate amounts. Immediately after the last injection of vaccine the patient complained of severe headache, pains and numbness in the thighs and arms, blurred vision, restlessness and complete insomnia. A retrobulbar neuritis of both eyes was detected and there was absence of abdominal reflexes. On 3rd February, 1945, the patient was completely blind in both eyes, but by the end of February his eyesight was almost normal. Recovery was recorded as complete by the first week of March. Vitamin B_1, 50 to 100 mgm. per day, cod-liver oil and liver extract had been administered. The author states that to his knowledge this is the first time that optic neuritis has been recorded in association with anti-rabies vaccine treatment, but the editor of the journal adds a footnote that he is aware of one other case, not referred to in the literature, in which an optic neuritis was ascribed to the effects of such treatment.

(vi) *Miscellaneous.*

CASALS[9], in a paper read to the American College of Physicians of New York, gave a useful summary of the present state of knowledge with regard to rabies. He covered such points as the incidence of the disease in animals and man in America, diagnostic methods, prevention and control, including vaccination methods. Much of the ground covered has already been referred to in recent reviews of American literature [this *Bulletin*, 1943, v. 40, 200–202, 269, 653, 655–6; 1944, v. 41, 173, 179–181; 1945, v. 42, 170].

It is obvious that the author, like many of his fellow countrymen, considers that the incidence of rabies in the U.S.A. is a blot on their escutcheon. During a period of 15 years the number of cases of rabies in human beings has averaged 55 a year, and from 1936–40 there were known to be at least 10,000 cases per annum in animals in the U.S.A. The continued potential danger is much greater than these figures might imply. He stresses the necessity of control of the disease in dogs, by application of muzzling orders, destruction of stray animals, and strict quarantine orders. Such control, he states, is within the functions of the Public Health officials. [As already pointed out in the reviews on rabies in this *Bulletin*, great headway is not likely to be made unless a uniform policy for the control of the disease in the whole of the U.S.A. is adopted, this

[8] KOENIGSFELD, E. G. H. Neuroparalytic Accident following Anti-Rabic Vaccination. *J. Roy. Army Med. Corps.* 1945, Nov., v. 85, No. 5, 254–5.

[9] CASALS, J. A Current View of the Rabies Problem. *Ann. Intern. Med.* 1945, July, v. 23, No. 1, 74–8.

control to be in the hands of the Bureau of Animal Industry, who would have to have the co-operation of the police. The Public Health authorities would take the necessary measures with regard to treatment of human beings. The reviewer understands that this could only be effected by altering the Laws of Congress, but surely this is not an insurmountable difficulty. At present each State has its own policy of control, and in most cases the police apparently believe that responsibility for control lies with public health officials only.] CASALS[9] states that Australia is kept free of disease by enforcement of quarantine laws. He is not accurate when he says that " in England relaxation of the ordinances on muzzling and leashing has been found to result in a sharp increase in the number of cases of rabies," as can be confirmed by reference to the last review on rabies [this *Bulletin*, 1945, v. 42, 680–682]. [Great Britain, like Australia, is favourably placed geographically with regard to control of the disease, and the regulations in force require all canines and felines landed in Great Britain from abroad to be quarantined for a period of six calendar months after landing, on premises approved by the Ministry of Agriculture. Outside quarantine kennels no cases have been confirmed since 1922, and the disease is likely to be introduced only by criminal evasion of the quarantine regulations. Only when the occurrence of the disease outside kennels was confirmed would muzzling and leashing orders be applied.]

HABEL[10], in his very comprehensive paper recording the results of well controlled experiments in guineapigs, mice and monkeys, strongly suggests that further consideration should be given to seroprophylaxis, either alone or combined with vaccine, in anti-rabies treatment. As he points out, seroprophylaxis in rabies should theoretically be highly effective provided protection is in part or entirely due to circulating antibodies, since the time of exposure to infection is known, and the incubation period is often prolonged sufficiently for active immunity to be produced before the virus has established itself in the vital centres in the C.N.S. Yet in the U.S.A. little attention has been given to this method of prevention. The author has reviewed some of the earlier work on anti-rabies serum in which conflicting results were obtained, but the experiments were made on only a few experimental animals and were inadequately controlled. During more recent years, from 1934 to 1939, workers, notably in Rumania and India [see this *Bulletin*, 1934, v. 31, 642 ; 1935, v. 32, 180, 610–612 ; 1937, v. 34, 235 ; 1938, v. 35, 173 ; 1939, v. 36, 727] have considered the question of serum prophylaxis in rabies and have carried out experiments in guineapigs, rabbits and monkeys to test the effect of anti-rabies serum. These same workers have also reported on the use in man of serum alone and serum combined with vaccine. The present author, by applying more recent methods of testing the potencies of virus, antiserum and vaccine, has extended these observations and presented the problem in a new light. His main conclusion, which would appear to be well justified, is that his experimental results in animals warrant a trial of immune serum either alone or combined with vaccine, in prophylactic treatment of the disease in man. He makes suggestions for the application of serum prophylaxis based on the results of his experiments, which differ from anything that has been tried before, *viz.* : (1) Anti-rabies serum alone would be administered in those cases of infection now requiring only 14 doses of vaccine, *i.e.* cases of doubtful infection ; (2) immune serum followed by commencement of a course of vaccine treatment 6 days later, in those cases now requiring 21 doses of vaccine. It is known that a large number of people at present receiving vaccine treatment against rabies have not definitely had an exposure to virus infection and they

[10] HABEL, K. Seroprophylaxis in Experimental Rabies. *Pub. Health Rep.* Wash. 1945, May 18, v. 60, No. 20, 545–60, 3 figs. [34 refs.]

are thus exposed to the discomfort, and in some cases possible unpleasant sequelae, of vaccine treatment. This has been considered necessary as early treatment is indicated, and diagnosis of the disease in the biting animal is not always definite. However, by employing mice for the diagnosis of the disease in the biting animal it is now possible to get a reliable answer to the diagnostic test in 6 days. If the result is negative, no vaccine need be given and the patient would have only had one dose of serum. On the other hand if the result is positive, vaccine treatment would be commenced. In the latter case the serum could act in two ways, by local destruction of the virus and by retarding the spread of the virus in the C.N.S., as evidenced by the present experiments in which the incubation period was prolonged even although the animals did not prove to be completely protected. This prolongation of the incubation period is probably just what is required for the vaccine to be effective (it would appear that in many failures in vaccine treatment the incubation period is short), hence the better results in the animal experiments with a " street " strain of virus when serum and vaccine treatment were combined, with an appropriate interval of 6 days between the two. The use of serum locally at the site makes possible specific treatment while the virus is localized. The author describes a method for the preparation of an anti-rabies serum and concentration of the antibodies, and no doubt this could even be improved upon. It would be impossible to discuss all the details of the author's experiments in a short review. *Ian A. Galloway.*

BARANOVSKAYA, S. A. [**Prolonged Passage of Rabies Street Virus in White Mice.**] *Zhurnal Mikrobiologii, Epidemiologii i Immunibiologii.* Moscow. 1943, No. 12, 76–8. [In Russian.]

LEGEZYNSKI [this *Bulletin*, 1939, v. 36, 725] has stated that street virus and fixed virus behave differently on serial passage in white mice, in that the former could only be passed 4–6 times, while fixed virus went through 56 passages without loss of virulence, and that this difference was sufficiently constant to be used as a means of differentiating between the strains.

In the course of routine passage of various strains of street virus in white mice the author has accumulated data which are in opposition to the findings of Legezynski. Twenty cases of passage from human, dog and bovine brains to white mice are reported ; the virus could be taken through 10–30 passages without loss of virulence, while the incubation period soon fell to 5–7 days. Only in one case did the virus die out in the fourth passage. It is suggested that the difference between these results and those of Legezynski may be due to the fact that the latter was dealing with less virulent West European strains. *D. J. Bauer.*

MCDONALD, S. **A Method for the Demonstration of Negri Bodies.** *Indian J. Med. Res.* 1944, Oct., v. 32, No. 2, 205.

" 1. Fix thin slices of *hippocampus* and *cerebellum* in 10 per cent. formol saline for 24 hours and prepare paraffin sections in the usual manner.

" 2. Take sections to tap-water.

" 3. Stain with Weigert's iron-haematoxylin for 10 minutes.

" 4. Rinse in water and transfer to Masson's ponceau 2R-acid fuchsin, diluted 1 : 10 with distilled water, for 5 minutes.

Stock.—Ponceau 2R	... ...	0·7 g.
Acid fuchsin	... ...	0·35 g.
Glacial acetic acid	... ...	1·0 cc.
Aq. dest.	... ...	100·0 cc.

" 5. Rinse in water and transfer to 1 per cent. phosphomolybdic acid for 5 minutes.

" 6. If necessary, differentiate in 5·0 per cent. sulphuric acid till sections are bluish red. Rinse well in water.

" 7. Dehydrate, clear and mount in the usual manner.

" *N.B.*—(*i*) Stage 6 must be carefully controlled ; 2 or 3 minutes usually is sufficient but the exact shade can only be learned by experience, (*ii*) use the $\frac{1}{6}$ in. objective and artificial light, (*iii*) Negri bodies appear deep red, nuclei greyish black and cytoplasm pale mauve."

VEERARAGHAVAN, N. **A Protozoan Parasite of the Central Nervous System.** *Indian J. Med. Res.* 1944, Oct., v. 32, No. 2, 207–22, 48 figs. on 4 pls.

Certain structures which the author first observed in the brain of guineapigs inoculated with rabies " street " virus and later in naturally infected dogs, jackals, a calf and a cat and in guineapigs infected from the saliva of a human case, are interpreted as protozoa. The youngest stages, fine granules, some so small as to be hardly visible, are called spores. They occur in the cytoplasm of nerve cells chiefly of the mid brain. The next stage is the ring form 0·5 to 8·0μ in diameter. In this the chromatin usually occupies a central position and, contrary to the usual staining reaction of Giemsa stain, the cytoplasm stains red and the chromatin dark blue. The ring stage, by growth and multiplication of the chromatin, becomes a schizont which appears to divide into merozoites which, with developing schizonts, may fill the cytoplasm of the nerve cell. Eventually the cell ruptures and the merozoites are set free. It is not quite clear if the author intends to imply that the merozoites become spores and that the spores in the first place develop into small rings. In some cases cystic forms over 30μ in diameter were encountered outside the nerve cells. These appear to be filled with spores of varying size but the spores in any one cyst were uniform in size. The author considers the possibility of confusing the structures he interprets as parasites with encephalitozoon or toxoplasma. It is considered that the Negri bodies which may occur in the same cells as the forms described are also stages in the development of the parasite. The paper is illustrated by 48 microphotographs of the various forms magnified 700 or 840 times.

Apart from the somewhat unusual staining reaction already noted and the fact that no known protozoon produces such minute spores as those described, doubts as to the protozoal nature of the structures are not lessened by the statement that they are filterable and appear in the brains of animals inoculated with Berkefeld V and N filtrates. There does not seem to be sufficient evidence that a protozoal parasite is involved, but whether the spores and other forms represent stages in the development of the rabies virus or are wholly or partly the result of the action of the virus on the cell cytoplasm, as the Negri body is usually supposed to be, future researches alone can show. *C. M. Wenyon.*

JOHNSON, H. N. **Fox Rabies.** *Alabama State Med. Ass. J.* 1945, May, v. 14, 268. [Summary taken from *J. Amer. Med. Ass.* 1945, July 7, v. 128, No. 10, 763.]

Johnson says that whenever fortuitous circumstances have allowed wild canine species such as the fox or coyote to become abundant in a region where rabies is enzootic in dogs there is a constant threat of a serious epizootic of rabies. The gray fox species has become unusually abundant in several of the Southern states. During the past seven years fox rabies has been reported in Alabama, Arkansas, California, Georgia, Illinois, Iowa, Indiana, Kansas,

Kentucky, Louisiana, New York, Pennsylvania, North Carolina, South Carolina, Ohio, Tennessee, Texas, Virginia, West Virginia and Wisconsin. In certain areas where foxes were usually abundant true epizootics of rabies developed. In one county in which fox rabies was prevalent 2,900 dogs were vaccinated within a period of three weeks. Four dogs developed rabies after vaccination, all within a period of thirty days. It is probable that these dogs were exposed before vaccination. Fourteen foxes, later proved rabid, were killed by fox hounds which had been vaccinated, and none developed rabies. No further cases of rabies have developed among vaccinated dogs in this county. The author cites several other outbreaks of fox rabies. In most instances the actions of rabid foxes are quite characteristic. Foxes are normally timid and avoid human habitations; those killed while invading farmyards in daytime have consistently been proved rabid by laboratory examination. Of the fox specimens submitted to the Alabama State Health Department, 31 were reported positive for rabies in 1943 and 32 in 1944. Nine persons were known to have been bitten by rabid foxes in 1944. It is essential that action be taken to reduce the number of gray foxes in areas where rabies is present. It is not necessary or practical to attempt to exterminate foxes, but their number must be reduced to a level where contact infection from fox to fox will not be frequent enough to maintain rabies. For the protection of their dogs and of their sport, fox hunters should aid rather than oppose such control measures. It is important that the heads of foxes and other wild animals such as skunks and coyotes be sent to laboratories for examination, so that there will be definite evidence of the extent of the disease.

THOMAS, C. R. **Landry's Paralysis following Antirabies Vaccine, with Suggestions as to Treatment.** *Tennessee State Med. Ass. J.* 1945, July, v. 38, 209. [Summary taken from *J. Amer. Med. Ass.* 1945, Sept. 15, v. 129, No. 3, 236.]

Simple abrasions and scratches should be cleansed with soap and water, iodine and alcohol or with mercury bichloride. Cauterization is ineffective unless used within an hour after injury, and then it destroys only the virus remaining on the surface. The use of the cautery does not lessen the mortality but is thought to prolong the incubation period and for this reason is considered to be of value. Pure phenol destroys virus rapidly. Vaccine should be given following a bite if the animal dies or develops rabies within ten days; also if it disappears or is a stray. Because of the extremely short period of incubation in injury of the face, lips, head and hands, and in deep multiple lacerations, it is advisable to give vaccine immediately and in large amounts. It has been estimated that about 3 in 10,000 patients receiving this treatment develop some sort of paralysis. The commonest form of paralysis, except the very mild ones, is one which resembles the ascending type described by Landry. The author observed this type of paralysis in a man who stated that after the second injection of rabies vaccine he felt "hot all over," but he had no other symptoms until after the last injection, when paralysis was rapidly progressing, so that within three days he was unable to move his hands or feet, and in four days the arms and legs could not be moved nor could he raise his head. There was some muscle soreness in both upper and lower extremities but otherwise no sensory changes. He was admitted to the hospital. Hot compresses were applied and vitamins E and B_1 were given. From 100 to 300 mg. of thiamin was given daily, both the oral and intravenous routes being used. Wheat germ oil was given orally for the first three weeks. For about three weeks the case seemed hopeless. The patient began to be able to detect a little movement in the big toe on the right and then the muscles of his neck became stronger, then

the muscles of his back, and after eight or nine weeks he was able to sit alone. He was given daily hydrotherapy treatment, massages and so on for about two months. His progress has been slow but steady. He can now walk without crutches and can hold light things in his hands. At present he is taking 30 mg. of thiamine daily and swimming three or four times a week. In the past month he has been able to take a light job. Perhaps he is one of a group who would have got well eventually, regardless of what was done, even though he was getting steadily worse until treatment was instituted.

Remlinger, P. Los fracasos del tratamiento antirrábico. [**Accidents in the Treatment of Rabies.**] *Rev. Sanidad e Hig. Pública.* 1945, Sept., v. 19, No. 9, 589–97.

Mullett, C. F. **Hydrophobia : its History in England to 1800.** *Bull. History of Med.* 1945, June, v. 18, No. 1, 44–65. [Refs. in footnotes.]

MALARIA.

Peset Aleixandre, T. & Romeo Viamonte, J. M. Estudio de las marismas del Guadalquiver desde el punto de vista de su endemia palúdica. [**A Study of the Country round the Lower Reaches of the Guadalquivir in relation to Endemic Malaria.**] *Rev. Sanidad e Hig. Pública.* 1945, Oct., v. 19, No. 10, 687–700, 2 graphs.

Ackerknecht, E. H. **Malaria in the Upper Mississippi Valley 1760–1900.**

This book is reviewed on p. 261.

Russell, P. F., Rao, T. R. & Putnam, P. **An Evaluation of various Measures of *Anopheles* Larva Density.** *Amer. J. Hyg.* 1945, Nov., v. 42, No. 3, 274–98, 9 figs.

" Various expressions of *Anopheles* larva density have been computed by simple and by partial correlation technique. The data were collected in a survey covering 33 months, from June, 1937, through February, 1940, in Pattukkottai Town and Taluk, Tanjore District, Madras Presidency, India, a recently opened rice field area where *A. culicifacies* is a prolific breeder as well as the malaria vector. The analysis was applied to data pertaining to larvae of this species and to those for all *Anopheles* larvae captured in the area. It has been shown that :

" 1. Good correlation exists between the logarithms of the monthly captures and either collection unit, minutes, or square feet. The relationship is, therefore, exponential in character.

" 2. When regression equations expressing the relationship between larvae captured and both minutes and square feet are computed, the minutes spent dipping are found to be the determining factor. Area covered does not contribute to the number of larvae captured when time is held constant. Captures in wells during 1937 and in borrow pits throughout the period are exceptions to this rule.

" 3. The precise form of the equation describing the relationship differs for larvae captured from different habitats. It also changes from one year to another.

" 4. For routine field use a simple ratio of larvae captured to minutes spent dipping furnishes a practicable measure of density."

Romeo Viamonte, J. M. & Irigoyen Ramirez, A. Nota previa sobre el anofelismo de la Zona del Protectorado español de Marruecos. [**Anophelines of Spanish Morocco.**] *Rev. Sanidad e Hig. Pública.* 1945, Oct., v. 19, No. 10, 669–74, 3 figs. on 1 pl. & 2 graphs.

Mohan, B. N. **Details of the Procedure adopted in maintaining a Laboratory Colony of** *A. fluviatilis.* *J. Malaria Inst. of India.* 1945, June, v. 6, No. 1, 75–6.

Since January 1944 a colony of *Anopheles fluviatilis* has been maintained at Mettupalaiyam, seventeen miles east of Coonoor.

It was started from eggs obtained from wild-caught females which were isolated in tubes containing damp filter paper. The eggs were floated in waxed, cork rings on water in mud-lined enamel bowls. For larval food, hay infusion was added to the water together with brewer's yeast or (when obtainable) a mixture of litmus milk (2 parts) and dehydrated blood serum (1 part). The water was aerated daily. Newly formed pupae were removed to bowls of clean water in a colony cage ($2 \times 2 \times 2$ feet) which was kept inside a larger one.

Humidity in the cage was maintained by hanging up damp cloths and providing a screened tray of saturated solution of common salt. For the adults glucose water on cotton wool was available and a rabbit with shaven back was put in the cage every night. The bred adults paired only in the presence of a blue light. The females laid their eggs on the water in mud-lined bowls and earthenware pots ; more in the pots than in the bowls.

Though the colony now appears to be flourishing it was observed that the females fed more readily on the rabbit after several egg layings ; it is therefore important that such a colony should be allowed to become well stocked and established before removing any mosquitoes for experimentation.

H. S. Leeson.

Keener, G. G., Jr. **Detailed Observations on the Life History of** *Anopheles quadrimaculatus.* *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 263–70, 3 figs.

The author worked with a large colony of *Anopheles quadrimaculatus* kept in cages in an institution in Alabama, and maintained under nearly constant climatic conditions (high humidity : air 76° to 80°F. : water about 4° lower).

The paper contains a large amount of fact, some of it not easy to summarize. Males and females emerge in approximately equal numbers, the males before the females—as in many other mosquitoes. The author gives information about the average duration of the early stages, including the separate larval instars. The time from laying of egg to emergence of adult is a mean of 21 days, and particulars for the duration of the several instars are given. As to the length of life of the female, it seems that 50 per cent. of them survive 21 days and the maximum is given as 62 days, but there are no particulars as to how they were fed, whether they were mated, and so forth. Pairing takes place most commonly at about 8 p.m. (season and natural illumination not stated), the insects being then extremely active. The female can pair either before or after a blood meal and can then lay several batches of fertile eggs, though there is no statement as to whether fertility falls off gradually after a single pairing. The insect takes about 3 cmm. of blood at a meal, and during the first few days of life occasionally feeds more than once in the 24 hours. The female deposits eggs while she is standing on the side of the bowl close to the edge of the water, the eggs appearing at the tip of the abdomen and being jerked off into the water singly, at intervals of a few seconds. Five females

were kept singly and averaged over 200 eggs per batch, some of them laying nine to twelve batches, a figure which does not seem consistent with the statement that the insect may produce three to four thousand eggs.

The paper contains a large amount of valuable information; the quantitative material would have been more useful if the author had given original figures rather than percentages, and some indication of the consistency of results. All who have maintained colonies of *Anopheles* know that the differences between successive experiments are often great. *P. A. Buxton.*

METCALF, R. L. **The Physiology of the Salivary Glands of** *Anopheles quadrimaculatus*. *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 271–8.

The author presents information on the anticoagulins and agglutinins in the salivary glands of *A. quadrimaculatus*.

Anatomically the glands resemble those of other species of *Anopheles*, with two lateral acini and one median acinus which is shorter. The lateral and median acini differ in the type of gland cell, and in the *p*H of the crushed acinus (lateral about 6, median about 7). The ducts, including those inside the acini, are lined with chitin (identified only by a blue-violet fluorescence).

The crushed whole gland of the female mosquito contains an agglutinin: this is much stronger in the median than the lateral acinus, and develops when the insect is a few hours old. It is active, even at one in a million, on corpuscles of many sorts of mammal, including men of several blood groups, but is not active on chicken or turtle blood. The glands of the female also contain an anticoagulin, active at dilutions of one in ten thousand. The agglutinin and anticoagulin are thermolabile.

Females of other species of *Anopheles* examined by the authors, and by other workers, contain essentially similar salivary agglutinins and anticoagulins. Females of a number of Culicines contain neither. Males of *A. quadrimaculatus* contain neither.

The glands of female *A. quadrimaculatus* appear to contain no digestive enzymes: protease, lipase and amylase could not be demonstrated.

P. A. Buxton.

BRADLEY, G. H. & FRITZ, R. F. **Observations on Seasonal Occurrence and Abundance of** *Anopheles quadrimaculatus* **Say.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 251–62, 12 figs.

The authors have tabulated a very large amount of fact on adult *Anopheles quadrimaculatus* in the U.S.A., particularly the South and East. They are concerned mainly with the season in which adults occur in catching stations, and with their numbers. Data are graphed against average annual temperature, and the county is divided into zones at 5°F. intervals. In the warmest zone (70–75°F.; *i.e.* peninsular Florida, southern Texas and Louisiana) adults occur all through the year, and the same is almost true in the 65–70°F. zone. In the third zone (60–65°F.) there is a definite absence of adults from houses during the four winter months, and this period is longer in the next two isothermal zones. The maximum number which may be taken in a catching station is not, apparently, very different in the five zones: maxima at the peak month run from about 1,000 to 5,000 per catching station. In the colder parts of the country, with annual means below 50°F., no "significant" numbers of this insect are recorded. [As a rough way of tabulating a large amount of information the method seems to justify itself.] *P. A. Buxton.*

Eyles, D. E., Sabrosky, C. W. & Russell, J. C. **Long-Range Dispersal of** *Anopheles quadrimaculatus*. *Pub. Health Rep.* Wash. 1945, Oct. 26, v. 60, No. 43, 1265–73, 3 figs. (2 on pls.)

The authors have investigated the range of flight of *Anopheles quadrimaculatus* round a certain very large breeding place in South Carolina. Circumstances were unusual, and marked mosquitoes were frequently recovered over two miles from the release point ; the extreme figure was 3·63 miles, measured of course in a straight line.

The paper is full and well recorded (though the map has no scale). Some 3,500 mosquitoes marked with aluminium powder were released at one point on a single day in the centre of a very large swamp. Owing to the extent of the swamp there were no catching stations or domestic animals within two miles. In all, 21 of the marked mosquitoes were recovered (in some 40,000 caught and examined). The authors point out that even within one species of mosquito, range of flight is influenced by a great variety of factors. They do not regard these observations as contradictory to the generally held view that a one-mile limit of control is generally satisfactory for *A. quadrimaculatus*. They conclude that areas must be studied individually. [For a similar experiment with *A. quadrimaculatus* in Delaware, see this *Bulletin*, 1945, v. 42, 687.]

P. A. Buxton.

Causey, O. R., Deane, L. M. & Deane, M. P. *Anopheles aquasalis* **vs.** *Anopheles tarsimaculatus* **as the Name for the Brackish Water Anopheline of Central and South America and the Caribbean Islands.** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 243–50. [18 refs.]

Miles, V. I. **Differentiating the Larvae of** *Anopheles georgianus* **King,** *A. bradleyi* **King, and** *A. punctipennis* **(Say).** *J. National Malaria Soc.* Tallahassee, Fla. 1945, Sept., v. 4, No. 3, 235–42, 3 figs.

Castillo, Roberto Leví. **Los anofelinos de la Republica del Ecuador.** Vol. 1.

This book is reviewed on p. 262.

Schultes, W. Bedeutung der Sternalpunktion in Diagnose und Rezidivprognose der Malaria. [**The Value of Sternal Puncture for Diagnosis and Prognosis in Malaria.**] *Münch. med. Woch.* 1944, July 28, v. 91, Nos. 29/30, 384–5.

Sternal puncture is a valuable means of diagnosis in chronic malaria when parasites cannot be found in the blood or only after repeated examinations ; by its use the author found trophozoites in 66 (51·5 per cent.) of 128 cases of clinical malaria in soldiers. It is also useful for prognosis as regards the likelihood of the occurrence of relapses and for judging the fitness of soldiers for active service after recovering from an attack of malaria. A further 176 patients, soldiers, were examined by sternal puncture after a course of atebrin [mepacrine] and plasmoquine [pamaquin] ; no plasmodia were found in 79, ring forms and dividing forms were present in 7 (they had no fever), half-grown and fully-grown parasites were found in 78, and gametocytes only in 12. In these cases no parasites were found in blood films.

The technique is simple and causes little pain, but experience is needed in the microscopical examination of the marrow preparations. *J. F. Corson.*

Bookless, A. S. & Naftalin, J. M. **Typhoid Fever complicated by Benign Tertian Malaria.** *Brit. Med. J.* 1945, Dec. 8, 804–5, 1 graph.

The authors have had under their observation recently 34 cases of typhoid fever, in two of which benign tertian malaria preceded by 17 days the onset

of typhoid and in ten others the two infections were present together. The cases were part of two small outbreaks, and among the first 8 patients *P. vivax* was found in the blood of two, but *none responded to antimalarial treatment* [our italics]. Again, in two only "did the temperature charts suggest double infection showing alternating hectic and remittent fever for the first four days." In others the fever at the onset was irregularly remittent.

The interest of this paper lies in the patients with concurrent infections of malaria and typhoid fever. There were, as stated already, ten such, and the course in four was mild, in three "moderate" and in three only was it severe; there were no fatalities among these, and only one patient had a relapse (not malaria). These figures are to be contrasted with the 24 plain typhoid cases, of which 12 were mild, 6 "moderate," 3 severe, and 3 fatal; 8 cases relapsed. It was noted that antimalarial drugs did not form an obstacle to positive haemoculture for *Bact. typhosum*. This was positive for 28 out of the total 34 cases. It is noteworthy also that "O and Vi agglutination tests were not carried out systematically." Thirdly, "patients with uncomplicated B.T. malaria always improved on quinine," state the authors. In the early stages of illness indications of so serious a disease as typhoid fever were absent, and the early diagnosis on clinical grounds was hindered [the authors' term] by the simultaneous presence of, or immediate recovery from, malaria.

[It is to be hoped that more of these cases will be reported, and many are likely to occur. The reviewer noted all the above facts 26 years ago (*Ann. Trop. Med. & Parasit.*, 1919, v. 13, 195–214 [this *Bulletin*, 1920, v. 15, 252]), but they seem to have been forgotten. Sir Patrick MANSON had noted earlier still that in malarious subjects the onset of typhoid is often preceded by three or four paroxysms exactly like those of ordinary ague and that the failure of response to quinine should put us on our guard. It is—it certainly *was*—regrettably far from uncommon for the tropical practitioner to give quinine to any patient with fever and only when fever continued in spite of the quinine did he begin to look for causes other than malaria. Again, any disease, pneumonia for example, in a malarious subject is apt to assume an intermittent or periodic character. Sometimes, as SCOTT has recorded (*ibid.*), the temperature chart may be that of straight malaria, but clinical signs of typhoid fever—rose spots, pea-soup stools, etc.—may be quite in evidence. The fact that no fatalities occurred among the authors' patients with the dual infection, and that 7 of the 10 were mild or moderate, corroborates the conclusion in the article referred to above, that cases of coincident enteric fever and malaria (even though each disease by itself is serious) often run a remarkably mild course. Incidentally, reference may be made to the remark of Sir Almroth WRIGHT of his having observed that antityphoid inoculation appeared to reduce the susceptibility to malaria. The subject of the antagonism of diseases is a very fascinating one and too little work has been done upon it. An interesting thesis, even a whole book, might profitably be written on the question.]

H. Harold Scott.

GELFAND, M. **Malaria in the European and in the African Patient.** *Clin. Proc.* Cape Town. 1945, Sept., v. 4, No. 7, 421–9.

PERRET-GENTIL, A. Essais de traitement de la malaria tertiana par la Vitaquine. [**Treatment of Malaria with Vitaquin.**] *Praxis.* Berne. 1945, July 5, v. 34, No. 27, 402–5, 3 charts. [13 refs.]

Vitaquine is a mixture of cinchona alkaloids, 40 per cent. of which are sulphates of quinine and hydroquinine, with a vitamin C preparation, Redoxo "Roche". Each tablet contains 0·2 gm. of the sulphates of cinchona alkaloids and 0·05 gm. of ascorbic acid. Twenty-five refugees suffering from

relapsing *P. vivax* malaria in Switzerland were treated with this preparation. A course of treatment consisted in the administration of 2 tablets three times a day, at meal times, for 5 days. After an interval of 3 days the course was repeated. Five or more such courses were given to some patients. Parasites disappeared from the blood on the 3rd or 4th day and the general condition of the patients improved. A certain amount of gastric irritation in some patients was relieved with colloidal aluminium hydrate or belladonna preparations. As the urine of most of these patients originally gave a negative reaction with dichlorophenol-indophenol, which was rectified by treatment, the administration of vitamin C appeared to be beneficial. *Norman White.*

Vollmer, H. & Liebig, H. Nebenwirkungen des Atebrins am Zentralnervensystem. [**Side Effects of Atebrin on the Central Nervous System.**] *Deut. med. Woch.* 1944, July 21, v. 70, Nos. 29/30, 415–17. [12 refs.]

The author refers to Geller's conclusions [this *Bulletin*, 1945, v. 42, 9] with which he disagrees, and records four cases of benign tertian malaria in which attacks of mania, and in one case temporary paralysis, were apparently caused by atebrin injected intramuscularly.

The first patient had five attacks of malaria in four months, the second, third and fourth of which were treated with quinoplasmine and no nervous disturbances occurred. In the first attack atebrin was given in doses of 0·3 gm. i.m. daily for 3 days, and 0·1 gm. orally *t.i.d.* for the next 4 days; after the second injection the patient showed mild maniacal excitement, and at the end of the oral course he had a severe maniacal attack which began suddenly and lasted for nearly three weeks. In his fifth attack of malaria mild mental disturbance followed the second injection of atebrin.

The second patient also had five attacks of malaria within a few months and all were treated with atebrin and plasmoquine. In the first, second and fourth attacks there were no nervous symptoms, but in the third attack the third injection of atebrin [presumably 0·3 gm.] was followed by the development of cramps, numbness and paraesthesia in the legs. His fifth attack of malaria was treated with double doses of atebrin —0·3 gm. i.m. *bis die* for two days, then 0·6 gm. orally for 5 days. In the night following the fourth injection the patient became acutely maniacal, four men being required to restrain him; on the following day he had hiccup, laryngeal paralysis and flaccid paralysis of the legs with diminished deep reflexes. He recovered quickly from the mania but the paralysis lasted for about ten days.

The third patient was treated for his first attack of malaria with double doses of atebrin—0·3 gm. i.m. *bis die* for three days. In the night following the third day, he got out of bed, ran across a yard barefooted to the office and demanded to be shot dead immediately; a few minutes later he became violently delirious, requiring eight men to hold him. No other neurological symptoms developed.

The fourth patient had three attacks of malaria in three months. The first two attacks were treated with atebrin, 0·3 gm. i.m. daily for three days, then 0·1 gm. orally *t.i.d.* for 4 days, and no nervous symptoms developed. His third attack was treated with double doses—0·3 gm. i.m. *bis die* for two days. In the next night but one after the last injection he wandered aimlessly about the hospital. Treatment with atebrin, 0·6 gm. daily by mouth, was continued, Luminal [phenobarbitone] being also given, and there were no further mental disturbances.

The authors add that such attacks are rare; the first patient was one among 350 treated with the usual daily dose of 0·3 gm. of atebrin, but the other three were among over 100 patients treated with double daily doses. Treatment

was not interrupted but was continued by oral administration and the authors think that their results justify this decision. [See also this *Bulletin*, 1945, v. 42, 253, 343 and 695.] *J. F. Corson.*

ZELIGS, M. A. **The Management of Chronic Malaria between Attacks, with special reference to the Effect of Nicotinic Acid on Malarial Headache.** *J. Amer. Med. Ass.* 1945, Nov. 17, v. 129, No. 12, 796–8.

Many members of the fighting services contracted malaria while in actual combat against the enemy. Chills and fever were an accompaniment of battle weariness, hunger, intense fear and exposure to wet and cold. After removal of such patients from the field, the febrile attacks could be readily cured, but symptoms such as easy fatigability, irritability, loss of weight, headache, backache and disturbed sleep, were liable to persist. This condition was often described as "post-malarial asthenia." The description is not apt. Malaria may play a part in the causation of the condition but so do the physical and psychological stresses of combat, and possibly also other tropical infections such as amoebiasis and ankylostomiasis. After return to the United States, and three months of reconditioning, malaria infections may persist but "asthenia" is very rare. The term "post-malarial asthenia" should be abandoned.

There are, however, certain symptoms so constantly associated with chronic malaria as to incriminate the malaria parasite as the cause; most common of these is malarial headache. This headache is usually bifrontal, mild to moderate in severity, never hemicranial, has no neurological prodromes, occurs on rising in the morning and usually improves after the patient has been up for a few hours. Prolonged persistence of malarial headache may produce secondary "neurotic-like" phenomena. The sufferers are not relieved by the usual headache remedies. Twenty-five selected patients were treated with nicotinic acid, 100 mgm. by mouth. The headache was relieved in 10 cases; there was moderate improvement in seven cases and no improvement in eight. No parasites were found in the blood, and there is no record of antimalaria treatment. *Norman White.*

RUPPOL, A. Paludisme, enfance noire et quininisation au Cercle de Gombe-Matadi en 1938 1939. [**Malaria, Native Children and Quininization in the Gombe-Matadi Region of the Belgian Congo in 1938–1939.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 82–9.

In 1938 the author examined thick smear blood preparations taken from a number of children in three villages that had previously been outside the range of activity of any medical organization. The children were considered in the villages to be enjoying normal states of health, though a child without an enlarged spleen was very exceptional. In 1939, infant welfare centres were at work and infants were given prophylactic quinine, 0·25 gm. four times a week; in that year the blood of all infants who were ill and who needed medical treatment was examined. The results of the blood examinations in the two years are given in detail and compared. In 1938 the blood of 16 out of 17 infants below the age of 6 months, and of all older children up to 5 years, contained malaria parasites. *P. vivax* was rare; *P. falciparum* and *P. malariae* were both abundant. The *P. falciparum* gametocyte index of these infants up to 5 years was 52 per cent., the *P. malariae* gametocyte index 54 per cent., the *P. vivax* gametocyte index 4 per cent. Mixed infections were common. In 1939 the parasite index was but little reduced, but the parasite density was markedly less. The gametocyte index was 50 per cent. lower, mixed

infections were rare, and quartan infections were much fewer except during the first six months of life. These improvements are attributed to the distribution of prophylactic quinine. *Norman White.*

PHILIP, M. I., RAMAKRISHNA, V. & RAO, V. V. **Turmeric and Vegetable Oils as Repellents against Anopheline Mosquitoes.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 343–4.

The authors have observed that in the Jeypore hill tracts, and on the Madras coast, spleen rates in boys are much higher than in girls. They think that this must be due to girls being less bitten by *Anopheles* than boys, and therefore less infected with malaria. This in turn is attributed to the fact that girls and women apply turmeric and vegetable oils to their bodies daily. In cage experiments an application of turmeric and mustard oil, subsequently washed with water but without soap, is repellent to hungry *Anopheles* of several species.

[It is one thing to repel in a cage experiment, quite another to find something which will remain even moderately repellent after rubbing on garments and for several hours.] *P. A. Buxton.*

MEDICAL ADVISORY DIVISION, HEADQUARTERS, SUPREME ALLIED COMMAND, SOUTH-EAST ASIA. **Trials of Malaria Control in South East Asia. Second Introductory Report. Indoor Spraying with D.D.T.** 3 mimeographed pp., 2 figs. [Undated.] **D.D.T. Report, No. 5. Indoor Spraying with D.D.T.** [SCHARFF, J. W., Colonel, Med. Adv. Div., S.A.C., S.E.A.] 51 mimeographed pp., 2 photos. [Dated 23rd Oct., 1944.] **D.D.T. Report No. 6. D.D.T. Air Spray Trial at the R.A.F. Station, Jessore. September, 1944** [SCHARFF, J. W., Colonel, with Senior WHITE, Major, I.A.R.O. (Med.).] 8 mimeographed pp., 1 plan. [Dated 23rd November, 1944.] **D.D.T. Report No. 7. Third Introductory Report. Air Spray Trials, Tamu Area, October, 1944.** [Entomological data furnished by MACAN, T. T., Major, R.A.M.C. Summary prepared by LAMBERT, J. D., Major, R.E.] 3 mimeographed pp., 2 figs. [Dated 23rd November, 1944.]

These papers constitute between them a lengthy report on the early trials with DDT in the Far Eastern theatre of war, to test its value in the control of mosquitoes, both adult and larval, for the protection of troops against malaria. All the trials were of the field type. For destruction of adult mosquitoes a 5 per cent. solution of DDT was applied, usually by means of a power driven sprayer of the paint spray type, the average dose of DDT per square foot of wall surface was 56 mgm., the huts treated were both thatch and of permanent construction, and the mosquitoes concerned were *Anopheles subpictus*, *A. annularis*, *A. hyrcanus*, *A. culicifacies* and *A. pallidus*. The normal procedure was to select a suitable group of houses, and to establish catching stations in them, in which periodical mosquito counts were made ; all dwellings were then sprayed, the catching stations being reserved to the last, and counts were continued in the treated catching stations.

Catching stations were of two types—netted and un-netted. The former were completely open at night, but were closed by an arrangement of mosquito netting at dawn, thus imprisoning any mosquitoes in them ; they remained closed for some hours, until the count was made. It was intended by this means to avoid errors due to the early-morning migration of mosquitoes, though it was recognized that the method held them artificially in contact with treated surfaces from which they might otherwise have been repelled. The un-netted stations were ordinary open houses in which hand collections

were made some hours after dawn. Curiously, and for reasons not understood, the catches in the two types of stations were the reverse of what had been expected, being higher in the un-netted stations, from which the mosquitoes had an opportunity of escape, than from the netted ones.

An almost complete disappearance of mosquitoes was recorded during the month after DDT treatment, after which there was a steady increase in anophelines in un-netted stations though the numbers previously found were not reached for several months ; the results were better when every habitation within the area was treated. DDT exerted no repellent effect, but there was some inhibition of biting in rooms which had recently been treated, and it was found that *Culex fatigans* was more resistant than *A. subpictus*.

The various types of equipment which might be used for distribution of residual films were surveyed, and it was concluded that the " Kent " pattern (a pneumatic knapsack machine in the body of which a high pressure is initially obtained by means of a hand pump) was suitable, though it needed some modification ; the technique of application is described.

Larval mosquito control was carried out from the air, using Hurricane aircraft equipped with two tanks, each holding 250 pounds of 5 per cent. solution of DDT in kerosene ; and application was at the rate of two to three quarts per acre. Some of the applications were made from formation flights of several aircraft in line abreast. Complete immediate control of swamp-breeding anophelines (*A. hyrcanus* and *A. philippinensis*) was secured ; fully developed larvae did not re-appear for about 12 days after treatment, and this result was associated with a marked reduction in the adult mosquito prevalence in the neighbourhood. When the same method was applied to country in which streams, containing larvae of such species as *A. minimus* abounded, full destruction of larvae was not secured, owing to the shielding effect of overhanging vegetation. Nevertheless, the DDT remaining on this vegetation killed mosquitoes coming to lay, or newly hatched, and in consequence very effective control of adults was secured despite the incomplete larvicidal result. *G. Macdonald.*

Afridi, M. K. & Arthur, J. H. **Future Military Malaria Control.** *South African Med. J.* 1945, Oct. 13, v. 19, No. 19, 361–5, 2 charts & 1 map.

The title of this paper, " future military malaria control," is not really applicable to the subject matter, which consists of an account of the incidence of malaria and the measures taken for its control, on the Indo-Burma front during the years 1942 to 1944. Very high malaria rates were experienced in the first part of the campaign, though even then the control measures adopted were instrumental in avoiding a complete breakdown such as occurred in some areas where they were neglected. The anophelines incriminated as carriers were *Anopheles minimus, A. jeyporiensis* var. *candidiensis, A. leucophyrus, A. sundaicus* and *A. philippinensis*, one or more of which occurred in considerable numbers in most areas and almost throughout the year, the seasonal prevalence of each is shown in a useful histogram.

Drainage was considered to be the backbone of control, though adult destruction and larvicides were also used ; but despite these and a carefully organized system which covered the whole line of communications the incidence of malaria remained high, the chief incidence being among forward troops, to whom suppressive treatment had been given from the first. Failures in control among these troops were due to neglect to take mepacrine when on patrol, when they were away from the supervised parades at which it was administered ; to reluctance to use head nets which obstructed vision, and to dislike for, and inefficiency of, the original repellent cream, or even the later pyrethrin

creams and dimethyl phthallate. These last objections were finally overcome by the adoption of a $\frac{3}{8}$ in. mesh net which, when impregnated with dimethyl phthallate, afforded complete protection against mosquito bites for 72 hours, while, following the Australian demonstration of the efficacy of mepacrine, an educational campaign resulted in the growth of greater faith in it, and its more regular use.

Also in the later part of the campaign, DDT became available ; and this was particularly valuable when applied from the air for the control of breeding places made difficult of access by jungle or by enemy mines.

The authors consider that the introduction of DDT, and the use of mepacrine, and repellent "fish nets," stand out pre-eminently as advances in malaria control which they will profoundly influence in the future.

G. Macdonald.

Lozano Morales, A. Problemas prácticos de lucha antipalúdica. Estudio experimental de un nuevo larvicida. [**Practical Antimalarial Problems : Experimental Study of a New Larvicide.**] *Rev. Sanidad e Hig. Pública.* 1945, June, v. 19, No. 6, 413–24.

Exacloruro de benceno [benzene hexachloride, or hexachlorcyclohexane, $C_6H_6Cl_6$] is a white powdery substance insoluble in water. It was synthesized in England as long ago as 1820 but only recently have its insecticidal properties been recognized. The author has demonstrated its value as a larvicide. Laboratory and field experiments are described. Excellent results were obtained by the application of the powder, 1 per cent., mixed with road dust, to *Anopheles* breeding places. Suspensions in water, following Barber's method of distributing Paris green, also gave good results. *Norman White.*

Henderson, J. M. **Antimalaria Measures for the Protection of Military Personnel in Puerto Rico and their Applicability to Civilian Malaria Control.** *Puerto Rico J. Pub. Health & Trop. Med.* 1945, June, v. 20, No. 4, 419-45, 6 charts & 1 fig. [Spanish version 446–72.]

Coulston, F., Cantrell, W. & Huff, C. G. **The Distribution and Localization of Sporozoites and Pre-Erythrocytic Stages in Infections with** *Plasmodium gallinaceum.* *J. Infect. Dis.* 1945, May–June, v. 76, No. 3, 226–38. [14 refs.]

In a previous paper [this *Bulletin*, 1945, v. 42, 538] two of the authors described the development of sporozoites of *P. gallinaceum* in the skin and organs of chickens, following cutaneous and intravenous inoculations. In the present paper are recorded the results of the inoculation, into uninfected birds, of blood and of organ or tissue emulsions of infected birds, at varying intervals after the latter had received an injection, by mosquito bite or by syringe, of sporozoites. In chickens bitten by infected *Aëdes aegypti* none of the organs or the blood were infective during the first 36 hours. The muscles at the site of the bite were, however, infective. From the 36th to the 79th hours occasional infections were produced by the blood and some organs (lung, spleen, heart). After the 79th hour the blood and organs regularly produced infections. After intravenous injection of large numbers of sporozoites, the lungs, spleen, kidneys, liver, pancreas and muscle produced infections during the first 36 hours. The blood was infective at the 36th hour but was negative thereafter till the 82nd hour. At the 70th hour all tissues became infective. When suspensions of sporozoites from 130–200 mosquitoes were inoculated intravenously, the presence of sporozoites in the blood was demonstrated for 5 to 20 minutes by subinoculation, and up to 15 minutes microscopically.

Subsequently the blood was negative till 40 hours later. Infected mosquitoes were allowed to bite the tip of a chicken's wing. The tip was isolated by ligature after varying intervals and then removed. Even when only 45 seconds had elapsed before the ligature was applied, the birds became infected. In practically all cases the removed portion of wing produced infection when subinoculated to uninfected chickens. The result indicates that dispersal of sporozoites probably takes place by way of the blood stream. [These results may be compared with those observed in man by FAIRLEY and his colleagues, see this *Bulletin*, 1945, v. 42, 630.] *C. M. Wenyon.*

JACOBS, H. R. **Immunization against Malaria. Unsuccessful Attempts to increase Resistance of Ducklings to *Plasmodium lophurae* Infections by previous Injections of Materials containing the Forssman Antigen.** *Amer. J. Trop. Med.* 1945, Mar., v. 25, No. 2, 151–3.

In a survey of animals susceptible to malaria it was noted that those possessing Forssman antigen or hapten are generally not liable to malaria infection. In most animals the hapten when present occurs in the tissues, but in the sheep and goat it is present only in the erythrocytes, while in the chicken it occurs both in the tissues and the erythrocytes. It is noteworthy that the chicken is a striking exception to the rule of non-infectivity. An attempt was made to increase the resistance of ducklings to *Plasmodium lophurae* infection by administering, at intervals of a few days, subcutaneous injections of the hapten prepared from guineapig kidneys, horse kidneys and sheep erythrocytes. These were employed as fresh suspensions or extracts of various kinds, heated or unheated. In only one of the experiments, in which heated suspension of guineapig kidney was used, did there appear to be any protection. It was not possible, however, to obtain a like result when the experiment was repeated. The conclusion is that attempts designed to increase the resistance of ducklings to the infection have yielded largely negative results. *C. M. Wenyon.*

BLACKWATER FEVER.

BRÜCKMANN, G. & WERTHEIMER, E. **Lysis of Red Blood Cells by Tissue Slices.** *Brit. J. Exper. Path.* 1945, Aug., v. 26, No. 4, 217–24. [11 refs.]

This is an account of an attempt to reproduce the findings of MAEGRAITH *et al.* [this *Bulletin*, 1943, v. 40, 584] in regard to lysis of red blood corpuscles in the presence of tissue slices. The authors confirm that washed tissue slices haemolyse washed red cells. They find that such lysis is inhibited by heat but not by serum, potassium cyanide or mercuric chloride, and that pre-incubation of the tissues " shortens the induction period and results in more rapid lysis." The lytic power of tissue slices is not species-specific. The authors conclude that the lytic phenomenon depends on autolysis and stasis and is " not connected with normal or pathological blood destruction."

[PONDER (*J. Gen. Physiol.*, 1944, v. 27, 483), states that he had no difficulty in confirming the results of Maegraith *et al.* so far as the lytic effect of tissue slices was concerned. He found that the lytic agent was destroyed by heat, and by high and low *p*H. He agrees with the present authors that the lytic agent is not species-specific. Ponder considered that the tissue lytic agent was possibly similar to lyso-lecithin. The present authors disagree with this. The disagreement that exists concerning properties of tissue lytic agents is probably due, fundamentally, to the fact that there is, as yet, no well standardized biological technique for their investigation.] *B. G. Maegraith.*

TRYPANOSOMIASIS.

WEINMAN, D. & FRANZ, K. **Early Results of the Treatment of African Trypanosomiasis with Two New Arsenical Preparations (Melarsen Oxide and 70A). Preliminary Report.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 343–4.

Two new arsenicals were tested against sleeping sickness in Liberia :—(i) Melarsen oxide (supplied by Parke, Davis and Company), a trivalent arsenic oxide derived from the pentavalent Melarsen previously introduced into therapy by E. A. H. FRIEDHEIM [literature references not cited by the authors ; see this *Bulletin*, 1941, v. 38, 634 ; and *J. Amer. Chem. Soc.*, 1944, v. 66, 1775] ; and (ii) a substance designated as 70A (supplied by Dr. Harry EAGLE), the composition of which is undisclosed beyond the statement that it is a phenylarsenoxide. [*Cf.* EAGLE *et al.*, this *Bulletin*, 1945, v. 42, 15 ; EAGLE, *ibid.*, 354.]

(i) *Melarsen oxide.*

Oral treatment : 12 patients, 8 of whom showed evidence of neurological involvement (5 with trypanosomes in the cerebrospinal fluid), were treated with 3 mgm. per kgm. daily, for 5 to 8 days. The blood, lymph glands and cerebrospinal fluids were clear of trypanosomes by the end of the course, or, in some late cases, after a second course. The cerebrospinal fluid cell counts of the late cases fell after treatment in all instances, though one of these patients was subsequently judged to have relapsed, because four months after his second course the count was found to be higher than when examined the previous month.

Intravenous treatment : 8 patients, 3 with neurological involvement, were treated by 0·1 mgm./kgm. daily for 7 days. Results in early cases were similar to those obtained by oral treatment. However, 2 of the 3 late cases failed to respond. Nevertheless, the authors write that for maximal effect the parenteral route is preferable to the oral [this is not borne out by the data which they present].

(ii) *70A.*

This compound was tried in 10 patients, and the authors conclude that it " was effective in the early stage but neither prevented nor ameliorated cerebral involvement." [It seems rather odd to credit a compound with effectiveness against the early stage of a disease, whilst also charging it with inability to stem the progress of that disease.]

[The observation periods after treatment by Melarsen oxide apparently varied from 2 to about 4 months, and this is quite insufficient for proper substantiation of the authors' claim as to " the indisputable efficacy of Melarsen oxide in meningo-encephalitic cases." Their criteria of efficacy in cases of neurological involvement are inadequate, as for example in the significance which they attach to the fact that in eight such cases the cerebrospinal fluid cell counts, initially ranging from 65 to over 1,200, with an average of 357 cells per cmm., declined after treatment to a range of 7–556, with an average of 138. To give point to this criticism, the reviewer has applied Weinman and Franz's method of evaluating cerebrospinal fluid cell count changes to the data provided by HARDING in Table I (p. 107), of his paper on the effects of antrypol, tryparsamide and diamidines [this *Bulletin*, 1946, v. 43, 107]. In seven cases treated by pentamidine or propamidine in which the initial cell counts were, as in Weinman and Franz's late cases, above 65 per cmm., the counts in all individual cases were, as in Weinman and Franz's experience, reduced after treatment (4 to 6 months later), and the range of 74–536, with an average of 255, fell to a range of 3–17, with an average of 10 cells per cmm.

According to Weinman and Franz, therefore, pentamidine or propamidine would be judged highly efficacious in meningo-encephalitic cases, which in fact they are not.

With regard to 70A, it is disappointing to find, in a highly respected scientific journal, that space is allowed for a description of the unpromising results of therapeutic trials with a compound whose formula is not revealed.]

E. M. Lourie.

LEWILLON, R. Le piégeage expérimental de " *Glossina palpalis* " à la Mission Médicale du Kwango. [**Experimental Trapping of *Glossina palpalis* at the Kwango Medical Mission.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 45–57, 2 figs.

Tsetse flies breed so slowly that they can sometimes be almost exterminated by measures aimed at destroying the adult flies. The Harris trap was markedly successful against *Glossina pallidipes* in Zululand, but gave disappointing results elsewhere, especially against *G. palpalis*. Two traps devised by SWYNNERTON, one using a flat shaded screen as an attractant and the other containing an animal (bullock or pig) have had a limited success in Tanganyika and elsewhere.

An easily and cheaply constructed trap, made entirely from indigenous materials, and resembling in outline a man, is described here. The lower part is similar to the " crinoline " trap, and the insects enter this from beneath. They then fly upwards to the light, and find themselves trapped inside a hollow gourd pierced with numerous small holes to let in the light ; the gourd represents the " head."

When carefully sited in a heavily infested fly belt, this new " mannequin " trap caught many flies and subsequently reduced the density. It was much more successful than the Harris trap, and as good or better than the Swynnerton models ; it was also the easiest and cheapest to construct.

As an anti-sleeping-sickness measure, trapping is compared with prophylactic injections of Antrypol (four injections per annum). It is more expensive to treat one individual than to construct four traps. The author considers that trapping is often the more practical measure. *Kenneth Mellanby.*

MAZZA, S., MIYARA, S. & JÖRG, M. E. Investigaciones sobre enfermedad de Chagas. Naturaleza de la reacción conjuntival en primer período de la enfermedad de Chagas. Enfermos comprobados exclusivamente por demostración de leishmanias de *S. cruzi* en biopsias conjuntivales. [**Studies on Chagas's Disease. The Conjunctival Reaction in the Early Period. Leishmanial Forms of *T. cruzi* in the Conjunctiva.**] *Universidad Buenos Aires : Misión de Estudios de Patologia Regional Argentina (Jujuy). Publicación No. 69.* 1945, 152 pp., 163 figs.

In an article published in 1944 the authors gave an account of the histopathology of the conjunctiva in the early stage of Chagas's disease [this *Bulletin*, 1945, v. 42, 792]. The present work is a sequel and an amplification of the former. The authors start by describing the projection microscope they use for examining biopsy specimens of the conjunctiva—the Zeiss Ultraphot, and refer to the Fuess Orthophot and the Emil Busch Citophot. It is an adaptation of the trichinoscope to a microscope. The apparatus is depicted and the optical projection presented diagrammatically.

They then pass on to give very detailed descriptions of the histological changes in portions of the conjunctiva taken by biopsy from 20 patients. The ages of the patients varied from 5 to 63 years. In 8 of these the diagnosis

was in no doubt; in 7 trypanosomes were found in the blood and in the other xenodiagnosis was positive; in 5 others the Guerrero-Machado test was positive, but not the blood examination nor xenodiagnosis; in the remaining 7 none of these was positive and the diagnosis rested on the clinical history, the general appearance, and the histology of the sections made from the biopsy specimens.

With a view apparently of driving home their point the authors indulge in a good deal of repetition. A record of the details of one case may be reproduced here to acquaint the reader with the histological changes present.

From a man of 43 years, on the sixth day after he had been bitten on the right eyelid by an infective bug, a fragment of the conjunctiva was taken for section and examination. The changes are thus described: Marked alteration in the conjunctival structure due, in part, to inflammatory infiltration and in part to epithelial erosion. There is intense congestion, with haemorrhages, some localized, others more diffuse, and serofibrinous oedema. There is moderate perithelial infiltration with small dense collars of perivascular infiltration, constituting in places nodular masses, with fibroblastic proliferation and oedema. There is no leucocytic invasion, but atrophy with erosion and ulceration, and the vessels are intensely congested to form a sort of "telangiectatic granuloma". In the parts less acutely affected the nodules are smaller, but the same epithelial atrophy is seen. Cytologically, the usual types of cell associated with inflammatory processes are present, together with proliferation of histiocytes and some fibroblastosis mingled with myeloid infiltration and serofibrinous exudation. Among hyperplastic histiocytes there is a dense fibrin reticulum and thin connective tissue fibrils of the inflammatory new growth type. Certain parts showing the nodule formation show also multinucleate structures tending to a coagulative necrobiosis of the central connective tissue, in the interior of which are free leishmanial forms of *T. cruzi*. Leishmania are commonly present in the macrophages and a few were seen in the walls of the capillaries. [The whole work is embellished with photographs of the patients depicting the palpebral oedema, and with photomicrographs of the tissue changes beautifully reproduced.] *H. Harold Scott.*

LEISHMANIASIS.

Da Cunha, A. M. Infecções experimentais na Leishmaniose tegumentar americana. [**Experimental Muco-cutaneous Leishmaniasis.**] *Mem. Inst. Oswaldo Cruz.* 1944, Oct., v. 41, No. 2, 263–82, 26 figs. on 7 pls. English summary.

Working with recently isolated cultures of *Leishmania brasiliensis*, the author inoculated rhesus monkeys intradermally over the superciliary arches, or on the nose. The course of the infection varied according to the type of lesion produced. Usually only a local lesion developed, in one to two months, which healed in three to eight months. In some cases, however, involvement of the nasal mucosa occurred. When this happened it was not the result of direct extension from a cutaneous lesion, which may occur as has previously been reported, but was due to the spread of the infection to the mucosa by some other channel. The nasal lesions, which were in the form of nodules on the nasal septum, and polypi which completely shut off the naso-pharynx, showed no tendency to spread to the pharyngeal region. Though the cutaneous lesions healed, those of the nasal mucosa persisted. Dogs were also successfully inoculated in the skin of the nose. One agouti (*Dasyprocta agouti*), and

a monkey which had recovered from a previous infection, were inoculated without result. The author points out that the development of extensive nasal lesions in the monkey affords further proof of the individuality of *Leishmania brasiliensis.* *C. M. Wenyon.*

FEVERS OF THE TYPHUS GROUP.

VARLEY, Florence M. & WEEDON, F. R. **Application of a Quantitative Complement-Fixation Test to the Serum Diagnosis of Typhus Fever.** *J. Immunology.* 1945, Sept., v. 51, No. 3, 139–46. [14 refs.]

The authors describe the highly specialized technique employed in a new quantitative method of carrying out the complement-fixation test in the diagnosis of typhus fever. The method was devised by WADSWORTH, MALTENER and MALTENER in 1938, and is described by Wadsworth in his book, " Standard Methods of the Division of Laboratories and Research of the New York State Department of Health," 1939 ; Williams and Wilkins Co., Baltimore.

In the method the end point adopted is described as follows : " 50 per cent. haemolysis of the cells present as a standard of reference rather than the point of complete haemolysis. This renders evaluation of the results much more precise and satisfactory." A set of four charts for use in carrying out the test is reproduced. Preliminary trials are said to show that lytic or slightly anticomplementary properties of the normal serum used for diluting the antiserum under test do not influence the quantitative estimation of the amount of complement rendered inactive by the antigen-antibody mixture.

The new technique is not likely to appeal to workers other than those who have exceptionally complete laboratory facilities at their disposal.

John W. D. Megaw.

CIUCA, M., MESROBEANU, L., BADENSKI, A., MUNTEANU, G. & PARASCHIVESCU, N. L'antigène glucido-lipidique des Proteus X est le facteur responsable de la réaction Weil-Felix. [**The Gluco-lipid Antigen of** *Proteus X* **is the Factor Responsible for the Weil-Felix Reaction.**] Reprinted from *Rev. " Stiintelor Med."* Bucharest. 1941, Feb.–Mar., Nos. 2/3, 7 pp.

CIUCA, M., MESROBEANU, L., BADENSKI, A., FRANKE, M. & MUNTEANU, G. Contributions à l'étude de la toxicité de l'endotoxine glucido-lipidique du Proteus X. [**The Toxicity of the Gluco-lipid Endotoxin of** *Proteus X.*] Reprinted from *Rev. " Stiintelor Med."* Bucharest. 1941, Feb.–Mar., Nos. 2/3, 14 pp.

CIUCĂ, M. & MESROBEANU, L. II. Sur la structure antigénique des variantes du *B. proteus.* Caractères physicochimiques de l'antigène glucido-lipidique du *Proteus X19.* [**The Physical and Chemical Characters of the Gluco-lipid Antigen of** *Proteus X19.*] Reprinted from *Bull. Sect. Sci. Acad. Roumaine.* Bucharest. 1941, v. 23, No. 7, 310–20. [22 refs.]

SCHÄFER, K. H. Stoffwechseluntersuchungen an Fleckfieberkranken. [**Investigations into the Chemical Changes in Typhus Patients.**] *Deut. med. Woch.* 1944, July 21, v. 70, Nos. 29/30, 417–19, 2 figs. [20 refs.]

The author has studied the chemical composition of the blood and urine of several patients during severe attacks of typhus fever.

The pronounced fall in the chloride content of the urine during the acute stage of the fever was not accompanied by any evidence of chloride retention

in the blood ; there was, instead, an appreciable diminution in six of the eight cases investigated. In five of these six cases the serum-sodium range was 184–216 mgm. per cent. and the chlorine range was 284–334 mgm. per cent. No pronounced fall was observed in the serum calcium, which ranged between 8·2 and 10·0 mgm. per cent. The potassium content of the serum was considerably increased, especially in very severe attacks, in which the findings ranged between 28·4 and 74·5 mgm. per cent. in the second week of the illness.

The serum proteins were rather low in all the cases investigated ; during the second week they were 4·88–7·6 gm. per cent. The residual [non-protein] nitrogen was not greatly increased ; it was only 21 mgm. per cent. in a fatal case ; and in the other four very severe cases it was 45–63 mgm. per cent. during the second week. The author concludes that great increases, up to 100 mgm. per cent. or more, occur only in cases complicated by glomerulonephritis, which was common during some epidemics in extremely cold weather.

The findings, especially in connexion with the chlorides, suggested changes in the permeability of the capillary walls, associated with a diminution in the volume of the blood plasma and a resultant fall in the blood pressure. The condition is described as one of " transmineralization ". *John W. D. Megaw.*

Duensing, F. Über pathologische Fremdreflexe bei Fleckfieber-Encephalitiden von choreatisch-myoklonischem Gepräge. [**Unusual Pathological Reflexes of Choreiform-Myoclonic Type in the Encephalitis of Typhus Fever.**] *Der Nervenarzt.* 1944, Mar.–June, v. 17, Nos. 3/6, 73–80. [10 refs.]

Two cases are described in detail, in which the patients suffered from a choreiform-myoclonic syndrome after attacks of typhus fever. The abnormal reflexes were of a type that the authors had never seen except in athetosis, myoclonus, and occasionally in Parkinsonism after encephalitis. The condition persisted for at least 14 months, and though there was some improvement by the end of that time it seemed unlikely that complete recovery would ever happen. *John W. D. Megaw.*

Gärtner, W. Erkrankung von Tonussteuerungszentren bei Fleckfieber. [**Affection of the Tonus-Controlling Centres in Typhus Fever.**] *Der Nervenarzt.* 1944, Mar.–June, v. 17, Nos. 3/6, 80–86.

The author describes and discusses at length a peculiar case of mental disorder which began 17 days after defervescence from a severe attack of typhus fever. The symptoms were varied and at different times suggested schizophrenia, hysteria, and hypnosis.

The main drift of the author's argument is that the manifestations resulted from damage to the nerve centres of the mesencephalon which control various mental, chemical, and mechanical functions of the body.

The patient was observed for four months, and although he had made a complete physical recovery his mental condition was still far from normal. The author stresses the need for an investigation by a psychiatrist in all cases in which a soldier commits offences against discipline after having suffered from typhus fever. *John W. D. Megaw.*

Raettig, H. Die fraktionierte Rekonvaleszentenserumbehandlung des Fleckfiebers. [**The Treatment of Typhus Fever with Fractional Doses of Convalescent Serum.**] *Med. Ztschr.* 1944, Nov., v. 1, No. 2, 59–60.

Having had unsatisfactory results from single large doses of convalescent serum the author decided to try small doses given daily by the intravenous

route. The treatment was started as early as possible and was continued till defervescence. At first the doses were 20–40 cc., but later they were increased to 40–60 cc., and better results were obtained with the larger doses, especially in severe attacks.

In a large number of cases treated in this way the case-fatality rate was 7·5 per cent. as compared with a rate of 18·3 per cent. among control patients. Although alternate controls were not employed the author insists that patients in whom the onset was specially severe were selected for the treatment and that the number treated (more than 300) was so large that the element of chance was eliminated. *John W. D. Megaw.*

Le Gac, P. Un cas mortel de typhus tropical constaté en Haute-Côte-d'Ivoire. [**A Fatal Case of Tropical Typhus in the Upper Ivory Coast.**] *Méd. Trop.* Marseilles. 1942, June, v. 2, No. 6, 473–7.

The clinical features of a sporadic case of typhus-like fever are described ; the patient died on the 12th day.

The Weil-Felix reaction was tested on the 10th day ; *Proteus OXK* was feebly agglutinated at a titre of 1–50, the *OX19* and *OX2* strains were not agglutinated. A Patas monkey and two rabbits were inoculated with the patient's blood, each animal received 5 cc. by the intraperitoneal, and 1·0 cc. by the intraocular route. Iridocyclitis was caused in the monkey and in one rabbit which also had a febrile reaction, but injections of its brain substance caused no reaction in a monkey, two rabbits, and two white rats. In the Weil-Felix responses in the originally inoculated animals, the highest titres were 1–80 in one rabbit against *OX19*, and 1–100 in the monkey against *OXK*.

The author regarded boutonneuse and " tick " fever as being excluded because the patient had neither the " very characteristic massive eruption," nor the *OX2* reaction observed in these fevers. He concluded that the disease was " related to Malayan typhus or the jungle typhus of Bengal."

[The evidence in support of a diagnosis of mite-borne typhus and against that of tick-borne typhus does not appear to be convincing, but judgment can be reserved because the author states that 15 other cases from different parts of the Upper Ivory Coast are being studied.] *John W. D. Megaw.*

Topping, N. H. **Tsutsugamushi Disease (Scrub Typhus). The Effects of an Immune Rabbit Serum in Experimentally Infected Mice.** *Pub. Health Rep.* Wash. 1945, Oct. 12, v. 60, No. 41,1215–20.

Serum of rabbits immunized by rickettsiae of tsutsugamushi disease was found capable of preventing the death of mice infected by lethal doses of homologous strains of rickettsiae. The serum was injected subcutaneously and was effective in some cases, even when given up to 72–168 hours after the time of infection. Serum of one of the four rabbits used was relatively ineffective. Large doses were more effective than small.

The rabbits were immunized by intravenous injections of infected yolk-sac material given on two consecutive days weekly for three weeks, and the serum was collected 19 days after the last injection.

The antibody content of the serum was increased by a further series of injections given after a resting period of several weeks.

Tsutsugamushi disease is regarded as specially favourable for serum treatment because of the possibility of immediate diagnosis at the time of onset in many cases owing to the presence of the eschar.

The author mentions that he has already found penicillin ineffective in the treatment of infected white mice, and that Andrewes, King and van den

Ende have had similar negative results with para-sulphonamido-benzamidoxime hydrochloride. [For the results of this drug in experimental typhus, see this *Bulletin*, 1945, v. 42, 20.] *John W. D. Megaw.*

Finnegan, Susan. **Acari as Agents transmitting Typhus in India, Australasia and the Far East.**

This book is reviewed on p. 262.

YELLOW FEVER.

Díaz, I. Brote de fiebre amarilla selvática en Venezuela durante el año 1944. [**Outbreak of Jungle Yellow Fever in a Venezuelan Area in 1944.**] *Bol. Oficina Sanitaria Panamericana.* 1945, July, v. 24, No. 7, 589–96, 1 map. English summary.

" An outbreak of jungle yellow fever occurred in an area close to the Andean range in the States of Barinas, Bolívar and Táchira, in Western Venezuela, near the Colombian border. First suspicions of the presence of the disease were aroused by the examination of a viscerotomy specimen from a patient from Cuite, who died on July 22, at the Hospital Vargas, of the city of San Cristóbal in the State of Barinas. It was also found out that in the section of San Cristóbal-La Colorada highway, several fatal febrile cases with blood vomiting had occurred about the same time. The chief of the Yellow Fever Division of the National Department of Health proceeded on September 3, 1944 to the area in question with a laboratory worker and an entomologist. A total of 12 cases of yellow fever, all of the jungle type, were verified by viscerotomy in areas completely separated in the three States involved. Two of the cases were in the State of Barinas, located in an oil camp in a jungle zone between the Andean range and the Barinas plain. In the State of Táchira nine fatal cases were verified and 21 other cases were studied clinically and epidemiologically, which were confirmed as yellow fever by the mouse protection test performed in the surviving patients. In the State of Bolívar, so far considered the only endemic yellow fever zone in Venezuela, only one case was found in a jungle area near San Félix, on the Orinoco river. It is supposed that in the whole area affected there must have been about 120 cases with a 70 per cent. death rate. (The last two patients reported were from La Tigra, about 16 miles S.W. of Barinas and died in the Barinas hospital on November 29 and December 6, respectively.) Precautionary measures were immediately taken through the local Health Authorities, including a campaign against *Aëdes aegypti* in urban districts, temperature-taking of all travelers, checking by the health authorities of febrile cases admitted to hospitals, and general vaccination against yellow fever. By the end of the year 28,263 vaccinations had been made as follows : State of Apure, 3,162 ; Barinas, 5,000 ; Táchira, 17,342 ; Zulia, 1,357 ; Bolívar, 1,402. In the State of Bolívar 14,000 persons had already been vaccinated during the two previous years. This represents about 50 per cent. of the total population and leaves unprotected only the Indians deep in the jungle."

Polak, Marius Frans. **Vraagstukken der gele koorts. Epidemiologie en vaccinatie.**

This book is reviewed on p. 264.

WADDELL, Mary B. **Persistence of Yellow Fever Virus in Mosquitoes after Death of the Insect.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 329–32.

Aëdes aegypti were fed on marmosets or Cebus monkeys infected with jungle strains of yellow fever and subsequently tested for virus content by intracerebral inoculation into white mice.

The mosquitoes were then killed either by chloroform, ether, potassium cyanide or tobacco smoke, and after varying time intervals groups of five were tested for virus content.

It was found that after death of the mosquito from chloroform, most of the virus activity was lost in 30 minutes and was completely absent after 1 hour. On the other hand significant amounts of yellow fever virus were recovered from the bodies of mosquitoes killed by the other three methods two hours after being killed, and were still present up to 45½ hours in those killed by potassium cyanide. Virus was also recovered from *Aëdes aegypti* that had died of starvation, up to 25 to 41 hours after death.

Specimens of *Haemagogus equinus* and *H. spegazzinii* which had died spontaneously after feeding on infected monkeys, were collected at intervals of from 1 to 3 days and tested for the presence of virus ; it was recovered from mosquitoes collected within 24, 48 and 72 hours after death, the exact time of death being unknown.

The use of ether is recommended as the most satisfactory method of killing insects when it is intended to use them in attempts to isolate yellow fever virus. *E. Hindle.*

See also p. 255, HADDOW, A. J., **The Mosquitoes of Bwamba County, Uganda.**

SMITHBURN, K. C. **Experimental Studies on the Yellow Fever Protection Test.** *J. Immunology.* 1945, Sept., v. 51, No. 3, 173–89. [10 refs.]

In 1930 THEILER [this *Bulletin*, 1930, v. 27, 872] discovered that white mice were susceptible to yellow fever virus. This led to the development of the intracerebral neutralization test of Theiler [*ibid.*, 1933, v. 30, 714] and to the intraperitoneal test of SAWYER and LLOYD [*ibid.*, 1932, v. 29, 198]. The latter was the simplest method for estimating protective antibodies in human and animal sera, and was used on a large scale in epidemiological studies and in the evaluation of immunity produced by various vaccines. More recently, WHITMAN in Brazil with the intraperitoneal test [*ibid.*, 1943, v. 40, 534] and BUGHER in Colombia with the intracerebral test [*ibid.*, 1941, v. 38, 434] have devised modifications which have advantages over the standard intraperitoneal test.

For various reasons these tests proved unsatisfactory under the conditions present in Uganda, and it became necessary to find some satisfactory modification.

It is known that immature white Swiss mice are much more susceptible to the virus than older ones, the decline in susceptibility being rapid in the first three weeks of life but after that time slow. Infant mice are highly susceptible to intraperitoneal inoculation. This susceptibility decreases rapidly in the older mice, but can be enhanced 10- to 15-fold by a preparatory intracerebral injection of starch solution. The use of younger mice also means that less serum can be used than is necessary in standard tests with 6-week-old mice.

Smithburn found that not only were 7-day-old mice more susceptible than older mice to the virus, but also that antibody protects against more units of effective virus in them. Similarly in 14-day-old mice the titre of antibody in

a known immune serum was twice as high against 10 times the number of effective units of virus as it was in 35-day-old mice. This suggested that smaller amounts of antibody would be detected if weaker virus was used in the immature mice.

It was found that a serum which gives an inconclusive result against a relatively strong dilution of virus will give fully protective results if the balance between virus and serum is not too heavily weighted by the former.

In sera which had previously given inconclusive results with the standard 10 per cent. virus test, tests with 1 per cent. virus indicated that an occasional serum which originally gave a protection ratio of 0/6 may be protective ; that if one mouse survived originally there is an even chance that the serum is protective ; and that if more than one mouse survived it is almost certainly protective.

The final test decided on in Uganda uses 1 per cent. virus, instead of 10 per cent. as used by Sawyer and Whitman. If 3·0 ml. or more of serum are available, the tests are done in groups of six mice 5–6 weeks old. They receive an intracerebral inoculation of 2 per cent. starch solution, and almost immediately afterwards receive intraperitoneally 0·6 ml. of a mixture of 3·0 ml. serum and 1·5 ml. of 1 per cent. virus. The mixture is not incubated prior to inoculation. If less than 3·0 ml. serum are used, the test is done in groups of 8–10 fourteen-day-old mice comprising two litters. They do not receive starch inoculation. Each mouse receives 0·06 ml. intraperitoneally of a mixture of 0·5 ml. of serum and 0·25 ml. of 1 per cent. virus. The results of these tests are interpreted as follows: If not more than 1 mouse dies the serum is considered protective. If not more than 2 mice survive, the serum is regarded as non-protective. If more than 1 mouse in a group die and more than two survive, the result is regarded as inconclusive. Re-tests are made on such sera whenever enough is available. *F. O. MacCallum.*

BUGHER, J. C. **The Effect of Prolonged Storage of Sera on Yellow Fever Protection Tests.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 333–8, 2 figs. [11 refs.]

Yellow fever immune sera that had been stored in glass ampoules at Yaba, Nigeria, under very unfavourable conditions for more than 12 years, were tested by means of the intraperitoneal protection test. Although the average loss of protective power seems to be about 50 per cent. each year, there were considerable individual differences and some of the sera still contained demonstrable antibodies. On the other hand in some instances the deterioration may be greatly accelerated. The velocity of deterioration seems to resemble that recorded by GLENNY in the case of diphtheria antitoxin [see *J. Hygiene* (Camb.), 1913, v. 13, 63].

Previously negative sera stored under the same conditions gave uniformly negative results. [See also this *Bulletin*, 1945, v. 42, 800.] *E. Hindle.*

DENGUE AND SANDFLY FEVER.

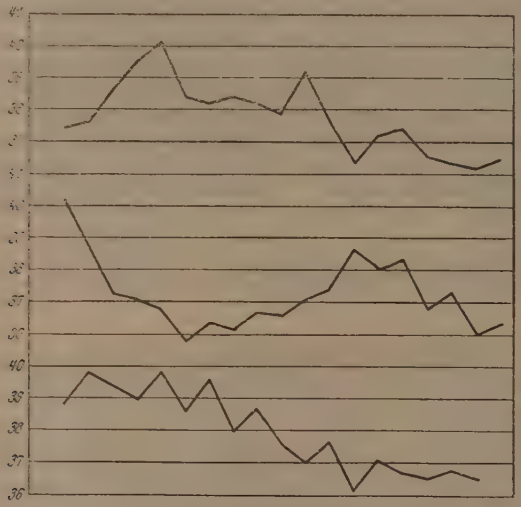
GOLDECK, H. & WALTHER, R. Zur Frage des Russischen Kopfschmerzfiebers. [**An Enquiry into Russian Headache Fever.**] *Klin. Woch.* 1944, Feb. 19, v. 23, Nos. 5/8, 59–61, 3 figs.

This paper contains additional information regarding the problem fever, " Russian headache fever", which is stated to have been common on the

" eastern front " during the recent war. No reference is made to the original description of the disease by SCHULTEN and BROGLIE [see this *Bulletin*, 1944, v. 41, 127].

The author mentions the occurrence of 6 severe and 12 mild cases of the disease among 36 Russians in one camp. He saw about 50 cases, but deals specially with 10 severe " meningeal " attacks in which stiffness of the neck was a prominent feature. The duration of the fever was 3–5 days in six ; 7 days in two ; and 8–10 days in two.

The cerebrospinal fluid was sterile on culture ; it contained a considerable amount of albumin and numerous white cells, mostly lymphocytes ; the cell count ranged from 37 to 1,070 per cmm. It is stated that even in the mild cases the white cells were increased, the counts ranging from 10 to 100. The headache is described as being localized in the occipital region. There was pronounced bradycardia.



Temperature Curves in " Russian Headache Fever."
[Reproduced from *Klinische Wochenschrift*.]

The three fever curves illustrating the paper show a striking resemblance to types commonly seen in dengue or sandfly fever, and the author states that the curve was of the saddle-back type in more than half the cases.

No information is given with regard to epidemiological conditions connected with the occurrence of the disease ; even the seasonal distribution of the cases is not mentioned. *John W. D. Megaw.*

PLAGUE.

CORNIL, L., POURSINES, Y. & MOUSTARDIER, G. La peste expérimentale du cobaye et du rat blanc (données anatomo-cliniques). [**Morbid Anatomy and Histology of Plague in the Guineapig and Rat.**] *Méd. Trop.* Marseilles. 1944, Mar.–Apr., v. 4, No. 2, 111–29, 10 figs. on 4 pls.

Five guineapigs and six rats were used and were inoculated intraperitoneally, subcutaneously and subconjunctivally with suspensions of 48-hour sloped

cultures. A number of photographs of the histological lesions in liver, lungs, suprarenals, heart and kidney accompany the text. Three grades of acute lesions are distinguished. Necrosis and parenchymatous degenerations constitute the chief histological features in each organ and are recognizable in two types as toxic and septicaemic with abscess formation. *W. F. Harvey.*

MATHUR, W. & GOYAL, R. **The Treatment of Plague with Sulphathiazole.** *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8, 383–5.

Sulphathiazole has now become standard treatment in plague. It was used by the authors, in 81 out of 120 patients, along with some adjuvant treatment such as a tablet of nicotinic acid 15 minutes previous to each dose if nausea was pronounced, or 10 per cent. soluseptasine and 15 cc. of 25 per cent. glucose parenterally to combat toxaemia. Digitalis or coramine were additions if cardiac weakness set in. There were 17 deaths in all. *W. F. Harvey.*

CHOLERA.

SEAL, S. C. **The Problem of Endemicity of Cholera in Bengal. (A Plea for further Investigation.)** *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8, 414–17. [10 refs.]

The author has himself taken part in the important researches on the epidemicity and endemicity of cholera which have been conducted in India for very many years. Answers were, or are still, required to the questions: (1) What is a true cholera vibrio? (2) What is the best method of its recognition? and (3) What is its relation to other types of vibrio found in human beings, water, etc.? The Bengal Cholera Field Enquiry found that "*V. cholerae* could not be isolated from the stools of the general population or from water in the endemic area except in direct relation to the cholera case." Cholera is in fact transmitted from case to case, and close contact carriers or water are only allowed infective agency "for short periods and at short range." It is interesting to note that an area is classed as "endemic if during the last 32 years there were not more than 30 months in which cholera deaths were not recorded and if the maximum period of absence of cholera records was less than 5 months." Many questions are presented for solution and for the most part the conclusion is reached that a final verdict is still awaited. "The problem of primary importance in the epidemiology of cholera is the mystery involved in its endemicity." In question form this is put as: "Where and how does the cholera vibrio exist before a case occurs in the endemic area?" *W. F. Harvey.*

BINSON, G. Etude des principaux caractères de 94 souches de vibrions et de quelques épreuves utilisées dans le diagnostic bactériologique du choléra. (Note préliminaire.) [**Vibrio Characters and Tests for Cholera.**] *Méd. Trop.* Marseilles. 1944, Jan.–Feb., v. 4, No. 1, 32–48. [29 refs.]

A collection of 94 laboratory strains of vibrio were at the disposal of the author and have been tested diagnostically. They are classified as: (1) isolated from cholera cases; (2) of indeterminate origin; (3) water vibrios; and (4) El Tor vibrios (true and Macassar strains). This is a preliminary note and takes up specially:—I. Biochemical reactions: (*a*) sugar fermentation and the classification of HEIBERG; (*b*) the cholera-red reaction; (*c*) the Voges-Proskauer test; II. Haemolysis; III. "OH" agglutination and the thermostability test of

Gipsen. These are for the most part standard tests. Some of the conclusions may be recorded briefly in serial order :—I. Heiberg's Group I is constituted essentially by agglutinable organisms from cases of infection with the true cholera vibrio. The cholera-red reaction is not a singular characteristic of the true cholera vibrio. A rather high probability value attaches to the Voges-Proskauer test in differentiating between the true cholera vibrio and the original El Tor, but an exception has to be made for the Celebes strain of Macassar. II. Haemolysis as a standard is much disputed, but affords a striking differential character, with sheep erythrocytes, capable of separating the non-haemolytic cholera vibrio from the haemolytic El Tor. III. Agglutination does not separate the haemolytic vibrios, especially the El Tor group from the non-haemolytic. The author lays very great stress on the Gipsen test because it is easy to carry out, easy to read and economical of time, which are very important considerations for the quarantine or frontier officer. This test is carried out as follows :—An 18-hour agar culture is made into a dense suspension in a normal salt solution. One-half of this suspension is heated at 56–57°C. for 3 hours and, when cool, a comparison is made of the agglutinability of heated and non-heated suspensions kept at 46°C. for 16 to 18 hours. Agglutination is read as being (*a*) with complete clearing, (*b*) with partial clearing, or (*c*) with no clearing of the suspension. El Tor vibrios are completely thermostable and still show complete clarification, whereas vibrios isolated from cholera cases are thermolabile, that is, clarify only partially or not at all. The test should be a boon to the epidemiologist, who has to apply detention measures to wayfarers with discernment. *W. F. Harvey.*

Panja, G. **An Easy Method of producing Permanent Rough Variation in Cholera Vibrios.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 342–3.

Rough colonies of Inaba and Ogawa subtypes of cholera vibrios were obtained by growing the smooth vibrios on a nutrient agar plate containing atebrin (Bayer) in a strength of 1 : 5,000. Rough colonies appeared after a few days and were replated on ordinary nutrient agar. Both variants appeared to be permanent. *J. F. Corson.*

Panja, G. & Ghosh, S. K. **Viability of Dysentery, Enteric and Cholera Organisms in Milk Curd** (*Dahi*). *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8, 390–92

Curdled milk or *dahi* is a universal food throughout India and it may be "sweet" or "sour". Both types contain lactic acid bacilli and have a *p*H ranging from 4·2 to 4·7. The efficacy of these bacilli or their acid product is widely appreciated. As a test, 4 drops of culture of dysentery, enteric and cholera organisms were severally added to about 10 cc. of dahi, and subcultures were made at fixed intervals. Cholera vibrios were killed within 5 minutes, typhoid bacilli in times varying from 5 minutes up to a maximum of one hour, while dysentery organisms required from 30 minutes up to 4 hours. An interesting comparison is made between lactic acid and other acids such as hydrochloric, acetic and citric with adjustment in all cases to *p*H 4·4. It was found that these other acids had a poor bactericidal effect by comparison with lactic acid on dysentery and typhoid organisms, and that all of them except citric acid were highly and quickly bactericidal to the cholera vibrio. Tests with lime juice showed that at *p*H 4·4 and in dilution it kills cholera vibrios in half an hour and undiluted (*p*H 2·8) in 5 minutes, but has no effect on *Bact. flexneri* or *Bact. typhosum.* *W. F. Harvey.*

BACILLARY DYSENTERY.

Bose, A. N., Sen Gupta, P. N. & Basu, U. P. **Sulpha Drugs in Bacillary Dysentery.** *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8. 385–8. [19 refs.]

It is generally accepted that the sulphonamide drugs, more particularly sulphaguanidine, sulphapyridine, succinyl sulphathiazole, phthalyl sulphathiazole and sulphanilyl benzamide, and even sulphanilamide itself, are more or less therapeutically beneficial in cases of bacillary dysentery. Sulphaguanidine is widely used, but it is costly and the dosage necessary is considerable ; its employment may be precluded by vomiting in those cases in most urgent need of it, as it cannot be injected. Furthermore, it is comparatively ineffective in *Bact. dysenteriae* (Sonne) infections. Sulphapyridine is effective, but causes nausea and vomiting, and, possibly, serious renal disorders if used in a dehydrating disease such as dysentery. Succinyl sulphathiazole is good, but again is inert against Sonne dysentery ; while phthalyl sulphathiazole is of low toxicity and is highly effective against Flexner infections. The activity of these acyl sulphathiazole drugs is dependent in part on their breaking down to sulphathiazole, or at least to some compound containing a diazotizable amino grouping in the system.

Sulphathiazole was found, by the authors, the best bacteriostatic agent of the series against a variety of dysentery organisms in culture ; sulphapyridine and sulphanilyl benzamide were found to approximate in activity to it, while phthalyl sulphathiazole was inferior to these but superior to sulphaguanidine. Succinyl sulphathiazole and sulphanilamide proved the least effective of these compounds when examined *in vitro*.

Sulphathiazole is relatively inactive against bacillary dysentery when given by the mouth, as it is readily absorbed from the gut. Succinyl and phthalyl sulphathiazole, prepared by acylating the *p*-amino grouping of sulphathiazole, are less soluble, less readily absorbed, and more therapeutically effective.

Sulphanilyl benzamide, although it is readily absorbed, has proved even less toxic but equally effective in the treatment of bacillary dysentery (including Sonne infections) in the hands of the authors, who therefore conclude that the activity of a sulphonamide in intestinal infections cannot be judged solely as an inverse measure of the degree to which it is absorbed from the gut.

Inquiries are proceeding to find out the factors on which the action of these drugs against intestinal infections depends. They think that sulphanilyl benzamide may be the drug of choice in the treatment of bacillary dysentery.

A. R. D. Adams.

Panja, G. **The Action of Drugs on Dysentery Bacteriophage.** *Indian Med. Gaz.* 1945, June, v. 80, No. 6, 294–5.

Experiments were made to see whether drugs used for the treatment of bacillary dysentery interfere with the action of dysentery bacteriophage. The drugs tested were : sulphapyridine, sulphaguanidine, soluseptasine, phenol, and electrolytic chlorine. The bacteriophage was used both concentrated and much diluted, and the drugs were used in two strengths, the sulphonamide in 1 and 2 per cent. solutions and suspensions, phenol in 0·5 and 1 per cent. solution, and chlorine in 0·25 and 0·5 per cent. solution. The drugs were kept in contact with equal quantities of the phage at room temperature for one or two hours, then filtered through L_3 candles ; the filtrates were tested for the presence of phage by their effect on cultures of dysentery bacilli on a solid medium. The details are shown in tables.

In addition to the experiments with drugs, dysentery phage was boiled for 2 and 5 minutes and tested similarly for activity.

The author concluded that these drugs have no action on strong dysentery phage, and that boiling a strong phage for 5 minutes does not completely kill it.
J. F. Corson.

AMOEBIASIS AND INTESTINAL PROTOZOAL INFECTIONS.

ENGLISH, R. B. **Carriers of *Entamoeba histolytica* in Africans of Northern Rhodesia.** *South African Med. J.* 1945, Oct. 27, v. 19, No. 20, 380.

In the Northern Rhodesian copper-mining town of Luanshaya, with a population of 2,500 Europeans and 30,000 Africans, dysentery is almost exclusively of the bacillary type, acute amoebic dysentery with trophozoites of *Entamoeba histolytica* being very rarely met with. Chronic amoebiasis in Europeans, however, appears to be becoming more common and causes anorexia, lassitude and inability to concentrate ; cysts are present in the faeces and the symptoms disappear with appropriate treatment. Because of this apparent increase among Europeans the author decided to determine the carrier rate among the African employees of the Roan Antelope copper mine.

Fresh preparations of faeces in saline and in Donaldson's eosin-iodine mixture were examined microscopically ; cysts of *E. histolytica* were found in 170 (33·4 per cent.) of the 509 Africans examined ; only 11 were " minuta " forms.

The author mentions, as interesting features of the local strain or strains of *E. histolytica*, that (1) few cases of true amoebic dysentery occur ; (2) hepatic or other amoebic abscesses rarely occur ; (3) trophozoites of *E. histolytica* are rarely seen in Africans even in the frequent stools passed when they are suffering from bacillary dysentery.

The local forms of *E. histolytica* appear to have low virulence but, since Africans are employed as domestic servants and handle food in European households, the high carrier rate among them represents a very definite public health problem. *J. F. Corson.*

PATEL, J. C. **Incidence of Amoebic Carriers in Bombay.** *Indian Physician.* 1945, Nov., v. 4, No. 11, 244–9. [23 refs.]

Out of 125 apparently healthy persons between the ages of 16 and 38 years, one faeces examination showed some protozoal and parasitic infection in 67 (53·6 per cent.) ; 54 (43·3 per cent.) had *Entamoeba histolytica*. In all these 54 cases the trophozoite stage was noted, though cysts were present in some. The presence of *E. coli* and other protozoa was not particularly sought for, but the former was detected in six along with *E. histolytica* and in four without. *Giardia intestinalis* was recorded three times and *Trichomonas hominis* once only. In nine cases ova of parasitic worms were found. The evidence available shows that, even though *E. histolytica* carriers, as in this series, are free from symptoms and are apparently healthy, they should be regarded as clinically infected and consequently should be treated.

[The high percentage of trophozoites of *E. histolytica* in so-called " carriers " is against the testimony of experience of most workers, and certainly deserves further investigation.] *P. Manson-Bahr.*

PATEL, J. C. **Incidence of Chronic Amoebiasis in Bombay and Non-Dysenteric Amoebic Abdominal Syndromes.** *Indian Physician.* 1945, Nov., v. 4, No. 11, 249–55.

During 1944, 101 stools of persons attending the Out-Patient Department of the Singhanee Hospital, Bombay, were examined. These patients were suffering from symptoms related to the gastrointestinal tract. The presence of *E. histolytica* was particularly sought for ; other non-pathogenic protozoa were not recorded. The dysentery amoeba was found in 58, in trophozoite form in 44, and in the cystic stage in 30 ; in 14, cysts alone were present. Of those with positive stools the youngest was six months old, the oldest 55 years. The symptoms, which varied in duration from a few days to 7 years, were as follows :—

Pain in the abdomen or diarrhoea ; vague pain, most in the epigastrium or in the right or left iliac fossa ; flatulence and abdominal discomfort, vomiting and hiccough ; low fever, lassitude, headache and giddiness ; lack of appetite, stomatitis ; pain in the chest and back, apathy and listlessness. In the case of females, irregular catamenia and excessive leucorrhoea ; loss of weight.

It is emphasized that chronic amoebiasis is more prevalent than is generally imagined, and is responsible for chronic ill-health.

[This paper represents the popular and widely-held attitude to amoebiasis and rests on a rather uncritical appreciation of symptoms which are common to a large section of the community in whom no evidence of protozoal infection can be obtained.] *P. Manson-Bahr.*

BIRNKRANT, W. B., GREENBERG, M. & MOST, H. **Amebiasis in a Hospital for the Insane.** *Amer. J. Pub. Health.* 1945, Aug., v. 35, No. 8, 805–14, 1 chart. [13 refs.]

In an investigation carried out in a hospital for the insane by the New York City Department of Health over a period of 15 months, 95 cases of amoebic dysentery were discovered among 5,575 inmates and employees. In mild cases diarrhoea was the chief, and often the only, symptom, blood being absent from the stools and there being no fever. In severe cases diarrhoea was marked and the stools were frequent, and in all cases blood was present ; many patients experienced abdominal cramps, and all had fever. Examination of 1,822 persons showing no symptoms revealed 124 carriers of *E. histolytica*. Examinations were carried out on iodine and saline preparations of fresh warm specimens and on material concentrated by the zinc floatation method of Faust. In all, 219 infections with *E. histolytica* were identified. Of these 61·5 per cent. were found on the first examination, the second, third, fourth and fifth examinations bringing the percentages to 80·5, 93, 97·6 and 98·5, respectively.

Patients with amoebic dysentery were taken into hospital and treated in the following manner. A daily injection of emetine hydrochloride (0·06 gm.) for three days, concurrently with chiniofon (12 tablets of 0·25 gm. each daily) for 10 days. After a 4-day rest period, carbarsone (one tablet of 0·25 gm. four times a day) was given for 10 days. In acute cases, as distinct from carrier cases, after a further rest period of four days, a seven-day course of diodoquin was instituted (12 tablets of 0·2 gm. each daily). This completed what is described as " intensive treatment " on the 35th day. It is stated that clinical and laboratory cure was obtained in all cases. Presumably this refers to the immediate result, for some months later there were 9 recurrences (or re-infections), 5 symptomless and 4 clinical cases. As regards infections among the inmates, these were particularly high in those with poor sanitary habits. Of

688 employees, 374 were inmate employees who gave an infection rate of 14 per cent., while the 314 paid employees gave a rate of only 6 per cent. It would seem inadvisable therefore to employ inmates in food-handling occupations. *C. M. Wenyon.*

KIRBY, H. *Entamoeba coli* **versus** *Endamoeba coli*. *J. Parasitology.* 1945, June, v. 31, No. 3, 177–84. [33 refs.]

In this article the author has attempted to settle the controversy which has been waged for some years over the use of the two generic titles—*Endamoeba* and *Entamoeba*. He, as others have done, advocates the use of the former for the amoeba of the cockroach and the latter for the well-known parasites of man [this *Bulletin*, 1945, v. 42, 327]. The following is his conclusion :—

" Opinion 99 of the International Commission on Zoological Nomenclature does not constitute proof that *Entamoeba* Casagrandi & Barbagallo, 1895 cannot be used as a generic name. Its argument rests on two points : that *Entamoeba* is a homonym of *Endamoeba* and that *blattae* is the type species of both, so that *Entamoeba* falls also as a synonym of *Endamoeba* Leidy, 1879. The latter point, which is the only one brought out in the summary of Opinion 99, is not acceptable : it rests on the interpretation that *Entamoeba* is a homonym of the earlier name. The Opinion asserts, but does not demonstrate, that it is a homonym ; and there is nothing elsewhere in the Rules or Opinions that warrants the assertion. It is appropriate to place the species *coli* and *blattae* in separate genera ; and it is considered that *Entamoeba* Casagrandi and Barbagallo, 1895, is available as a generic name for *coli* and congeneric species at the same time that *Endamoeba* Leidy, 1879, is used for *blattae* and congeneric species."

C. M. Wenyon.

SHIH LU CHANG. **Studies on** *Entamoeba histolytica*. **V. On the Decrease in Infectivity and Pathogenicity for Kittens of** *E. histolytica* **during prolonged in Vitro Cultivation and Restoration of these Characters following Encystment and Direct Animal Passage.** *J. Infect. Dis.* 1945, Mar.–Apr., v. 76, No. 2, 126–34. [31 refs.]

The author has studied two culture strains of *E. histolytica* from the point of view of their infectivity and pathogenicity to kittens. One strain lost its infectivity after 8 years of culture and remained non-infective for the following 3 years. The other strain became non-infective after 2½ years of culture. It was found that in both cases the loss of infectivity was associated with the cessation of encystment and that when encystment was again induced by transferring to encystment medium the infectivity was re-established. This infectivity, which was evident after administration of material either orally or intra-caecally, occurred only if the rectum was ligated. As plugging of the rectum was not sufficient, it is concluded that the ligation did more than merely stop the passage of the intestinal contents. It appeared to alter the physiology of the intestine. When the infectivity of the first strain was re-established it was found that, pathologically, it was as active as it was originally. In the case of the second strain the pathogenicity was much reduced. It was regained to some extent by rapid passage from kitten to kitten. The bacteria associated with a highly pathogenic strain of *E. histolytica* were administered concurrently with the amoebae which had ceased to be infective. This failed to re-establish infectivity. When such a strain had regained its infectivity the administration of the virulent bacteria concurrently with the amoebae appeared to encourage the production of more severe lesions. *C. M. Wenyon.*

Zuckerman, Lucile K. & Meleney, H. E. **A Fluid Medium for the Encystation of *Endamoeba histolytica* under reduced Atmospheric Pressure.** *J. Parasitology.* 1945, June, v. 31, No. 3, 155–7.

To prepare the medium, Cerophyl, a commercial product made from the dried leaves of young cereal plants, is extracted in CPR medium, which consists of cholesterol, one part per million, and Difco proteose peptone 5 per cent. in Ringer's solution. The Cerophyl powder is added to the medium in a concentration of 2 per cent. The suspension is autoclaved and filtered and finally distributed in 50 cc. amounts in 250 cc. Erlenmeyer flasks. Just before inoculation with amoebae, to each flask is added 5 cc. of inactivated horse serum and 0·02 gm. of specially prepared rice starch. After inoculation the flask is fitted with a rubber stopper and glass tube to enable the air pressure to be reduced to 40 mm. of mercury before incubation is commenced. It was found that without reduction of air pressure, multiplication of amoebae prior to encystment was limited. By the use of this medium for over a year, 100 flasks gave an average count of close on four million cysts per flask. *C. M. Wenyon.*

Meleney, H. E. **The Relationship of Clinical Amoebiasis to various Strains and Growth Requirements of *Endamoeba histolytica*.** *Puerto Rico J. Pub. Health & Trop. Med.* 1944, Sept., v. 20, No. 1, 59–70. [Refs. in footnotes.] [Spanish version 71–83.]

RELAPSING FEVER AND OTHER SPIROCHAETOSES.

Pavlovskiĭ, E. N. & Skruinnik, A. N. [**On the Period during which Females of *Ornithodorus papillipes* are able to transmit the Tick Relapsing Fever.**] *Zool. Zh.* Moscow. 1945, v. 24, No. 3, 161–4. English summary. [In Russian.] [Summary taken from *Rev. Applied Entom.* Ser. B. 1945, Nov., v. 33, Pt. 11, 165.]

Of a batch of 24 nymphs and adults of *Ornithodoros tholozani*, Lab. & Mégn. (*papillipes*, Bir.) taken in October 1931 in a cave near Stalinabad (western Tadzhikistan) and brought to Leningrad, 14 were alive in February 1933, ten in May 1934, six in April 1935, three (all females) in October 1940, and two in January 1941. During these years the ticks were allowed to feed at intervals on laboratory animals, and they transmitted spirochaetes of relapsing fever, with which they were naturally infected, to guineapigs and *Dyromys nitedula*. In September 1941, the two surviving females were sent in a thermos flask to Samarkand, where they arrived in October 1942. They had not fed for about two years, and one of them was dead in the following month. The other was taken back to Leningrad in June 1944, together with an adult male that had been found in western Kirghizia in 1935, and both were allowed to feed on a guineapig in October 1944. The latter subsequently showed spirochaetes in its blood, and as the male had failed to infect laboratory animals on any of the occasions on which it had fed alone, it is concluded that they were transmitted by the female.

Previous investigations by the authors have shown that *O. tholozani* can live for up to 25 years and can resist starvation for up to 7½ years. Its long life, the fact that spirochaetes persist in it from generation to generation, its wide range of hosts, other than man and domestic animals, and its tendency to move about little ensure the preservation in nature of foci of relapsing fever.

Wisseman, C. L., Jr. **Relapsing Fever in Denton County, Texas. Report on finding the Tick, *Ornithodorus turicata*, Naturally Infected.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 339–42, 2 figs. [10 refs.]

The author has succeeded in finding *Ornithodorus turicata*, infected with relapsing fever spirochaetes, in a cave near Roanoke, Denton County, Texas. It may be recalled that although this cave was suspected of being responsible for a number of human cases of relapsing fever [see this *Bulletin*, 1935, v. 32, 296] previous investigators had failed to find any infected ticks.

Three trips were made to the cave and each time ticks were collected from the sandy floor. Two members of the first party found ticks on their bodies, and seven days after being bitten one of them developed a typical attack of relapsing fever. Nine ticks were fed on a human patient undergoing pyretotherapy, and after five days he showed spirochaetes in the blood and had 4 relapses at intervals of 3 to 5 days. Spirochaetes were present during each febrile attack.

White rats were readily infected by the inoculation of blood from both human cases. *E. Hindle.*

Jarvis, J. F. **Relapsing Fever in an Infant of Five Days.** *East African Med. J.* 1945, Sept., v. 22, No. 9, 311.

An African woman was admitted to Morogoro Hospital, Tanganyika Territory, on April 9th 1945, developed relapsing fever on April 13th and gave birth to a child a few hours afterwards ; spirochaetes were present in her blood. The child remained apparently well until the 5th day, when it also developed relapsing fever and died next day in spite of having received a dose of 0·015 gm. of neoarsphenamine (N.A.B.).

The author thinks that the mother might have been infected in February as she gave a history of having had fever about that time ; or she might have been bitten by a stray tick while in the hospital between April 9th and 13th. He suggests that the child might have been infected from the mother through the placenta, or by entry of the maternal blood into an abrasion or the cut cord [could infection by a stray tick be excluded ?]. *J. F. Corson.*

Charters, A. D. **Louse-borne Disease.** [Correspondence.] *East African Med. J.* 1945, Sept., v. 22, No. 9, 308–9.

Wolman [this *Bulletin*, 1945, v. 42, 469] found that an Italian preparation of neoarsphenamine (Neo I.C.I.) had little effect on louse-borne relapsing fever in Addis Ababa, Abyssinia ; Charters, however, who used an allied arsenical preparation called " Neoical," at Sodda, Abyssinia, found that after a dose of 0·6 gm. intravenously clinical improvement took place within 24 hours, spirochaetes could no longer be found in thick blood films after 8 hours, and no relapses occurred. He suggests the following possible explanations of the difference in the results : (1) Wolman's patients were probably treated later in the attack than the author's, who were Gold Coast soldiers ; (2) some of Wolman's cases, regarded as " first attacks " may have been relapses ; (3) natives of the endemic district (Wolman's patients) may possibly respond less readily to the arsenical drug than new arrivals (Gold Coast soldiers). He think that the first explanation is the most important of the three. In his experience arsenical drugs have far greater effect on louse-borne relapsing fever than on the tick-borne form. *J. F. Corson.*

LEPROSY.

Bechelli, L. M., Keil, H. & Rotberg, A. Resultados da lepromino-reação em paises não endêmicos de lepra. (Nota preliminar.) [**The Lepromin Reaction in Countries where Leprosy is not Endemic.**] *Rev. Brasileira Leprologia.* São Paulo. 1945, Mar., v. 13, No. 1, 21–4.

Bargehr, de Langen and others in the Dutch East Indies have reported positive lepromin-reactors among apparently healthy individuals in contact with lepers, contrasting them with recent arrivals who do not react. It is inferred, therefore, that the lepromin reaction is an indication of a prior latent infection with production of specific antibodies. Children removed at birth from their leper parents react negatively.

The authors have tested the Mantoux reaction and the early and late lepromin reactions in patients at the Skin and Cancer Unit of the New York Post-Graduate Medical School, and suffering from conditions other than leprosy. Twelve had been born and had lived for part of their lives in places with very low leprosy incidence ; 36 had lived for a time in places where the disease was endemic. The results of each test are given in tables and the conclusions to be drawn from them are that a delayed lepromin reaction does not necessarily indicate a latent infection, but may be regarded as allergy to the lepromin injected 3–4 weeks before. Wade has remarked on the positive reaction to lepromin in persons who had not been previously in contact with lepers and he explained this by saying that such persons " can react allergically " to Hansen's bacillus when they come into contact with it. From the results recorded in the tables, the early reaction does not necessarily indicate either latent infection with leprosy, or sensitization to lepromin, for it may occur in 6–12 hours. It is thought that tuberculosis is responsible, for all but one of those tested who gave the early response were also Mantoux positive. The early lepromin reaction, therefore, must be regarded as non-specific and due to sensitization to *Myco. tuberculosis.* *H. Harold Scott.*

Amendola, F. A glândula lacrimal na lepra ocular. [**The Lachrymal Gland in Ocular Leprosy.**] *Rev. Brasileira Leprologia.* São Paulo. 1945, Mar., v. 13, No. 1, 3–11, 1 pl.

The lachrymal glands, orbital and palpebral, by continual secretion of tears when infected by leprosy, constitute an important focus of infection. Bacteriological examination often shows these to be infected in leprosy and their extirpation thus removes one focus of infection. In patients where other eye lesions are present, even though the glands do not appear to be involved, removal of them is often followed by marked improvement of these other lesions. This last was observed in three of the 20 cases briefly detailed in this paper. Thus, one, a woman of 18 years, had extensive keratitis of one eye and of one-third of the other, with photophobia and epiphora ; she was very depressed about her eyes and all kinds of medical treatment had been tried ineffectively. Extirpation of the lachrymal glands was performed ; histological examination of sections failed to reveal Hansen's bacteria. Nevertheless, a few days later the patient presented herself without pain or photophobia, happy and cheerful and hopeful of complete cure. Two months after the operation the benefit was maintained. The author is hopeful that the operation may prevent much of the suffering and ultimate blindness which now afflict so many lepers. *H. Harold Scott.*

Grau Triana, J. Exploración de poder oxido-reductor de la piel en la lepra. [**The Oxidation-Reduction Potential of the Skin in Leprosy.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1945, Oct., v. 2, No. 3, 154–8.

Julião, Oswaldo Freitas. **Contribuição para o estudo do diagnóstico clínico da lepra nervosa.**

This book is reviewed on p. 265.

González Prendes, M. A. & Ibarra Pérez, R. Duración de la lepra. [**The Duration of Leprosy.**] *Rev. Sifilografía, Leprología y Dermatología.* Marianao, Cuba. 1945, Oct., v. 2, No. 3, 175–9.

Duration of illness in this disease is very difficult to assess, as it depends on so many factors, among them the treatment adopted, whether it is begun early or late, whether it is carried out rigorously or half-heartedly, whether the surroundings are hygienically sound, whether the general state of health of the patient is good, the appetite, faith in the success of treatment and other matters. Jeanselme gives the duration as 10 to 20 years, Rodriguez up to 40 years. Miranda from a study of 552 patients who died, gives " an average of over ten years," and many have stated it to be over 20 years and occasionally as long as 40 and even 50 years.

The authors have tried to assess the average duration from a study of 270 cases. They found that 43·3 per cent. discovered symptoms between the ages of 16 and 30, and 15·1 per cent. between 16 and 20 years. The average age at which they became ill was 25·7 years, and assuming that the incubation period was five years [a big assumption], the average age at first infection is given as 20·7 years. In 121 cases (44·8 per cent.) the average duration was 16–25 years (including incubation) and 62 were in the 16·20 years group. The average duration of the whole 270 worked out at 23·15 years [we give the authors' figures ; they are not easy to reconcile with the details in the tables presented]. As extremes, one patient died in three years and another after 56 years' illness. The greatest number of deaths occurred between the ages of 36 and 45 years, with an average of 43·8 years. *H. Harold Scott.*

Lima, L. de S. & Cerqueira, G. de C. Terapêutica experimental da lepra pela soluthiazamida. Nota prévia. [**Trial of Soluthiazamide in the Treatment of Leprosy.**] *Publicações Médicas.* São Paulo. 1945, June–July, No. 154, 3, 5–7, 9–11. English summary.

Soluthiazamide is p. (γ-phenyl-propylamine) phenyl-sulphamido-thiazole-α-γ disulphonate of sodium. It is used in 45·3 per cent. solution, which contains 20 per cent. of thiazamide base. A 5 cc. ampoule contains 1 gm. of thiazamide. Most concentrated sulphonamides have a *p*H between 9 and 11·4 and this degree of alkalinity causes eschars ; soluthiazamide has not this drawback. Trials with it for leprosy have been going on for 8 months ; this is too short a time for a definite appraisement of its therapeutic value, but the results so far, as reported by the authors, are sufficiently promising to warrant more extensive testing.

Their clinical material comprised 100 cases, 50 with lepromata in a comparatively early stage and 50 adults with severe lepromatous forms and extensive involvement of the skin, in whom chaulmoogra had proved ineffectual. The drug was administered intravenously each day, except Sundays, for 3 weeks, the course being repeated after a week's interval ; the initial dose was 1 cc., which was increased gradually to 5 cc. and in adults to 10 cc. Those receiving more than 5 cc. were given also an equal amount of glucose solution.

The results observed so far comprise : cicatrization of leprotic ulcers and of conglomerate lepromata, disappearance of lepromatous infiltrations and softening of subcutaneous nodules ; perforating ulcers of the sole sometimes

improved and ocular symptoms, after a brief period of exacerbation, showed considerable amelioration and had not relapsed during the time that patients were under observation ; the nostrils became clearer, less obstructed, crusts disappeared and respiration was freer.

Examinations of the blood and urine were carried out systematically during the treatment. The red corpuscles were counted and the haemoglobin estimated before the treatment started and every ten days afterwards. If the red cells fell to 4 million per cmm., iron was given, if between $3\frac{1}{2}$ and 4 million, liver extract was ordered ; if lower still, soluthiazamide treatment was suspended and the anaemia treated until the blood returned to normal ; then it was restarted with small doses and gradually increased. If albumin or red corpuscles appeared in the urine the treatment was temporarily suspended. *H. Harold Scott.*

Possolo, Helena. **As flacourtiáceas antilepróticas.**

This book is reviewed on p. 266.

HELMINTHIASIS.

Burrows, R. B. **A Survey of Intestinal Parasites in Natives in Dutch New Guinea.** *Amer. J. Hyg.* 1945, Nov., v. 42, No. 3, 262–5.

Niño, F. L. Papel de los helmintos en las llamadas apendicitis verminosas. [**Worms found in so-called Verminous Appendicitis.**] *Bol. Inst. Clín. Quirúrg.* Buenos Aires. 1945, May, v. 21, No. 173, 277–81, 6 figs.

Ockuly, E. A. **Bilharziasis of the Bladder (Vesical Schistosomiasis).** *J. Urology.* 1945, July, v. 54, No. 1, 39–45, 1 fig. [25 refs.]

This is a record of the first case of urinary schistosomiasis detected at the Army Air Forces Regional Station Hospital No. 1 in Florida. The patient, a sergeant aged 22, was infected in North Africa or Sicily, was diagnosed cystoscopically as suffering from a tumour of the bladder, and was invalided to the U.S.A. The correct diagnosis was there eventually established by cystoscopic biopsy, and subsequently confirmed by the rather simpler procedure of urine examination, which revealed eggs of *S. haematobium.*

The patient was cured with Fouadin. The author discourses [at times loosely] on urinary schistosomiasis, and stresses the possibility of other members of the forces being found to be infected on their return to the United States. *A. R. D. Adams.*

Krakower, C., Hoffman, W. A. & Axtmayer, J. H. Granulación en la cubierta de los huevos de *Esquistosoma mansoni.* (Experimentación con cobayos esquistosomizados y alimentados con una ración deficiente de vitamina C.) [**Granulation of the Shell of the Ovum of** *Schistosoma mansoni.* **An Experiment with Infected Guineapigs fed on a Diet deficient in Vitamin C.**] *Puerto Rico J. Pub. Health & Trop. Med.* 1944, June, v. 19, No. 4, 669–78, 2 pls.

One hundred and thirty-nine guineapigs, each weighing 200–400 gm., were each infested with about 4,000 cercariae of *Sch. mansoni.* They were then divided into five lots. Four were given the following diet, deficient in vitamin C : Rolled oats 59 per cent., powdered skim milk, 30 per cent., heated in trays to 10°C. for an hour, 10 per cent. butter and 1 per cent. NaCl. Three of the lots

were given thrice weekly injections of ascorbic acid, the total weekly dosage being 3, 9 and 25 mgm. respectively ; the other lot had no vitamin. The fifth group was fed on green food.

All those on a scorbutic diet died within a month, or were killed at the end of that period, *i.e.* before oviposition had occurred. In these animals the parasite had undergone no change in growth or development ; the same was observed in the group receiving 3 mgm. ascorbic acid weekly. Disintegrated ova were rarely seen in those receiving 9 mgm. Of 50 animals showing the ovular changes 26 lived for more than 5–6 weeks after being infested ; the last one was killed after 109 days. Many of these guineapigs showed signs of scurvy, and in the 26 the schistosome ova seen in sections of tissue from the liver and lungs were disintegrating. The shells were swollen, sometimes laminated, eroded and granular, and around them histiocytes, giant cells, and perhaps lymphocytes, eosinophiles and polymorphonuclears. In the last stages the shells became granular, with greenish refracting granules, single or grouped.

To confirm these observations, a lot of 12 guineapigs, ten weeks after infestation, were gradually transferred from their green food to a scorbutic diet, and 7–9 days after being on the latter they were passing ova with disintegrated shells and these increased in number till at the end of four weeks half the eggs seen in sections of the liver had disintegrated shells. Such ova were very rarely seen in those receiving 9 mgm. ascorbic acid weekly, added to the scorbutic diet, and never in those on an antiscorbutic diet. Briefly, the effect of a scorbutic diet, or a diet with insufficient antiscorbutic addition, was to reduce gradually the number of eggs produced and the eggs themselves seemed to undergo a lytic process whereby the shell became granular while the surrounding tissue showed a certain degree of fibrosis. *H. Harold Scott.*

Hernández Morales, F. **Schistosomiasis Mansoni Manifestations of the Large Intestine.** *Puerto Rico J. Pub. Health & Trop. Med.* 1945, June, v. 20, No. 4, 492–8. [Refs. in footnotes.] [Spanish version 499–506.]

Hernández Morales, F. & Ruiz Cestero, G. **Roentgenological Changes of the Small Intestine in the Presence of** *Schistosoma mansoni*. *Puerto Rico J. Pub. Health & Trop. Med.* 1945, June, v. 20, No. 4, 507–10. [Refs. in footnotes.] [Spanish version 511–14.]

Elsaesser, K.-H. Zur Symptomatologie, Diagnostik und Therapie der Hirncysticerkose. Bericht über 8 Erkrankungen und tabellarische Zusammenstellung der Fälle des Schrifttums seit 1910. [**The Symptoms, Diagnosis and Treatment of Cerebral Cysticercosis. An Account of Eight Cases and a Table of Cases recorded since 1910.**] *Ztschr. f.d.g. Neurologie u. Psychiatrie.* 1944, July 25, v. 177, No. 3, 323–62, 8 figs. [Numerous refs.]

An article of much importance to all neurologists and not only to tropical practitioners. The author records in detail 8 cases of cysticercosis of the brain under his own observation and reviews a large number of cases reported in the last 34 years. The condition is very likely to be missed because the symptoms are not at all definite (see later) and even more because it is unsuspected ; he urges the importance of bearing the possibility in mind by those practising in districts where it is liable to occur and by any medical man called upon to treat patients who have been stationed, or have lived, in areas where the infestation exists.

At the author's clinic only 8 cases have been seen in the 12 years, 1931–42 inclusive, 6 in men and 2 in women. During that time some 20,000 patients have been seen, among them 2,500 neurological cases ; of these there were some 900 with signs and symptoms of cerebral tumour, so that there has been an average of one case of cerebral cysticercosis in every 125 of tumour.

There is no need here to detail the symptoms in each case ; there is a general type common to all, in which the symptoms are those associated with hydrocephalus in the adult : headache early and persistent, especially occipital and extending down the neck, giddiness, nausea and vomiting. These symptoms are usually aggravated by head movement, so the head is held steady, as a rule fixed to one side, and movement is restricted or carried out very cautiously. This goes by the name of the Bruns symptom. There may be affections of gait and of sensation, but these are rare and not in any way characteristic ; psychically, patients are mentally dull, but often euphoric. The duration of illness is difficult to assess because many show neurasthenic symptoms for some years which may, of course, have no connexion with the symptoms, psychic and other, due to the cysticercosis. Also, some patients have intervals of improvement, when symptoms may almost be absent for varied lengths of time. In a table of 63 cases with cysticerci situated in the basal meninges, the duration of symptoms is recorded as " short ", " several weeks " to as long as 26 years in one case recorded by GUILLAIN-PÉRISSON in 1927 [but not mentioned in the list of references]. Of these 63, forty (perhaps more) presented psychic disturbances of one kind or another. Others might be merely apathetic or show Korsakov's syndrome, paranoia, depression or hyperaesthetic emotional states.

Diagnosis is not easy, because symptoms are, in general, so vague. Rarely, lumbar, cisternal or brain puncture may result in finding fragments of a parasitic cyst. They tend early to calcify and then X-rays will reveal them. The cerebrospinal fluid may show 2–3 per cent. of the cells to be eosinophiles.

A favourite site for the cysts is the fourth ventricle. The author gives a list of 41 in which this was the case, and in a few there was a combination of fourth ventricle and basal meningeal infestation. Information in this list includes the name of the author reporting, the year of record, the sex and age of the patient, the chief clinical symptoms, and the duration of the illness so far as this could be determined ; it ranged from " a few days " to " perhaps 30 years." The ventricular cases are characteristically those which have an acute ending. The cysticerci are said to pass from the choroid plexus, to traverse slowly the third ventricle and the aqueduct and, having increased in size, are unable to penetrate the narrow slit-like lateral apertures to the foramen of Magendie. They are usually monolocular, rarely of the racemose type. If the cyst dies it becomes shut in by neuroglial fibrosis and then acts like a neoplasm. Pressure symptoms comprise a medium degree of papillary oedema on both sides, but only a few patients have serious disorders of vision ; in a fair number there is slight paresis of the 3rd and 6th cranial nerves ; cerebellar ataxy is seen in about one-fifth of the patients, epileptic attacks in one-tenth, but more in the basal meningeal cases than in those with ventricularly situated cysticerci. Operation is the only satisfactory line of treatment.

H. Harold Scott.

ANDERSEN, D. A. **Hydatid Cysts. A Clinical Study of a Short Series.** *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8, 373–7.

ROGER, H. Les kystes hydatiques du cerveau. [**Hydatid Cysts of the Brain.**] *Méd. Trop.* Marseilles. 1944, Mar.–Apr., v. 4, No. 2, 89–110, 7 figs. on 4 pls. [Bibliography.]

Mukerji, A. K. & Sen Gupta, K. K. **Effect of Heat and Light on the Ascaridol Content in Oil of Chenopodium.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 347–8.

Mukerji and Ghosh [this *Bulletin*, 1943, v. 40, 922] showed that when oil of chenopodium is kept at temperatures of from 70° to 98°F., whether exposed to light or kept in the dark, its ascaridole content decreases. To find the best way of storing the oil the authors of the present paper made experiments in which they kept samples in glass-stoppered bottles for one year under various conditions of temperature and exposure to light, the ascaridole content being determined at 2, 4, 6 and 12 months.

The smallest amount lost was in the samples which were kept in subdued light at 65° 75°F. and the authors conclude that oil of chenopodium is best stored in a cool place where the temperature does not rise above 75°F. and where there is protection from direct light. *J. F. Corson.*

Hernández Morales, F. & Diaz Rivera, R. **Poisoning by Carbon Tetrachloride and Oil of Chenopodium.** *Puerto Rico J. Pub. Health & Trop. Med.* 1943, June, v. 18, No. 4, 434 42. [Refs. in footnotes.] [Spanish version 443–51.]

Three cases of poisoning by a dose of a mixture of carbon tetrachloride and oil of chenopodium are described; the patients were white Porto Rican labourers aged 31, 36 and 35 years, respectively, and the circumstances were similar in all. Each man took a mixture of 2 cc. of carbon tetrachloride and 1 cc. of oil of chenopodium [a well recognized therapeutic dose] in the morning on an empty stomach, and immediately afterwards, took 60 gm. of magnesium sulphate. The first two men were admitted to hospital two days later and the third man three days later. In addition to the clinical examination, the urine and blood were tested at short intervals in the laboratory and the findings are shown in tabular form.

The symptoms were similar in all; an hour or so after taking the dose the patient had vomiting and diarrhoea with pains in the abdomen, headache and general body pains, and in two cases cramps in the arms and legs. Tenderness over the liver was present in all and two showed jaundice and enlargement of the liver, the lower edge being palpable three fingerbreadths below the right costal margin.

The urine was scanty in amount in all three but showed only traces of albumin and few casts, and the specific gravity was very low; the reaction was acid. In the third case, in which the effects of poisoning were the most severe, the amount of non-protein nitrogen of the blood is given as 200 mgm. per cent. on the day after admission, 300 mgm. four days later, declining gradually to reach 40 mgm. on the 25th day after admission.

The patients were treated similarly; they were given a high carbohydrate diet, calcium gluconate and glucose solution were administered intravenously and calcium lactate was taken by mouth. All recovered and were discharged from hospital on the 16th, 19th and 27th days respectively after admission.

The authors quote the views of various authors on the mode of action of the drugs and remark that it is difficult to decide which of the two drugs caused most damage, but they think that carbon tetrachloride caused most of the symptoms. *J. F. Corson.*

Dolce, F. A. & Franklin, J. E. **Creeping Eruption. Results of Treatment with Fuadin.** *Arch. Dermat. & Syph.* 1945, Sept., v. 52, No. 3, 174–5.

"The results of treatment with fuadin of 14 patients with creeping eruption were unsatisfactory in all but 2 instances."

BUCHANS, R. A. **Filariasis in the Armed Forces.** *J. Urology.* 1945, July, v. 54, No. 1, 59–61.

Before the recent war, Bancroftian filariasis was associated, in the minds of most medical men, chiefly with pictures of elephantoid scrota or limbs. The author states that these conditions result only from years of constantly repeated infection, and that few, if any, cases will be encountered in men of the U.S. forces serving in the South Pacific area. He wishes to allay the anxiety inspired by inspection of the text-book pictures by medical practitioners at home and by anxious relatives, of which he says " the end results on morale are terrific."

In actual fact the findings in men returned to the U.S.A. with a diagnosis of filariasis have been minimal, and he observes that sterility does not result from the infection. He offers some observations on the aspects of filariasis from the urological standpoint. *A. R. D. Adams.*

RAO, S. S. **Filarial Infection in Dhamda (Drug District, C.P.) due to** *Wuchereria malayi. Indian J. Med. Res.* 1945, May, v. 33, No. 1, 175–6.

Dhamda village is 21 miles north of the town of Drug, Central Provinces, India, and has a population of 3,628. The author took thick blood films between 9 p.m. and midnight from 120 persons in February 1942, and found microfilariae of *Wuchereria malayi* in 16 (13·3 per cent.). A survey of the village population at the time showed that there were 80 cases of elephantiasis of the legs or hands (2·2 per cent.), but no cases of hydrocele, chyluria, lymph varix or elephantiasis of the external genital organs were observed.

During the period of the survey the following mosquitoes were prevalent in the village : *Mansonioides annulipes* [=*longipalpis*], *M. uniformis*, *Culex fatigans*, and *Anopheles culicifacies*. All the big tanks were full of *Pistia stratiotes*, and *Mansonioides* bred there. Among the mosquitoes dissected *Mansonioides annulipes* alone showed filarial infection and this therefore appears to be the most important local vector. [See also this *Bulletin*, 1937, v. 34, 33 ; *Indian J. Med. Res.*, 1940, v. 28, 609.] *J. F. Corson.*

MCMARTIN, W. J. **Urological Aspects of Filariasis.** *J. Urology.* 1945, July, v. 54, No. 1, 62–74. [16 refs.]

After brief and lucid accounts of the history, geographical distribution, aetiology, pathology, symptomatology, diagnosis, psychiatric aspects and treatment of Bancroftian filariasis, the author cites six cases, of the many he has seen in service hospitals in the U.S.A., illustrative of the distribution of the lesions as classified by HUNTINGTON, FOGEL, EICHOLS and DICKSON (*Yale J. Biol. & Med.*, 1944, v. 16, 529).

He ends with the following reassuring conclusions :—

" Filariasis has infected thousands of our armed forces located in the Pacific area.

" The disease in these men is characterized by episodes of lymphangitis and lymphadenitis with the majority of the patients showing genital (scrotal) involvement.

" Civilian urologists will be confronted with the problems of differential diagnosis of intrascrotal pathological changes caused by filariasis as well as intrascrotal pathological changes usually encountered in the United States.

" There are many members of our armed forces who have filariasis and fear the onset of elephantiasis despite attempts of medical officers to dispel their fears. We can do a great deal to ease these patients' minds by educating them on the characteristics of the disease.

" There is no specific drug in the treatment of filariasis. Removal of the patient to a temperate climate and away from the chance of more infection is most important.

" Rest, elevation of the affected parts and cold applications is the treatment of choice in episodes of exacerbations of the disease.

" Research on the treatment of filariasis is constantly being carried out by very competent medical personnel of the Army and Navy. Excellent results of this work may be reported in the literature soon.

" Much will be added to the knowledge of the pathology of early filariasis when and if complete post mortem examinations can be done on patients who have filariasis, or who give a history of having had filariasis at some time during their life.

" Filariasis will not become a public health problem in the United States.

" Permanent disability as a result of filarial infestation among our armed forces will be a rarity.

" The Army and Navy Medical Corps have progressed rapidly towards eradicating this disease." *A. R. D. Adams.*

ROSE, H. M., CULBERTSON, J. T. & LIPMAN, Miriam O. **Antistreptolysin Titers in Cases of Filariasis with Recurrent Lymphangitis among Military Personnel.** *J. Clin. Investigation.* 1945, July, v. 24, 532. [Summary taken from *J. Amer. Med. Ass.* 1945, Nov. 17, v. 129, No. 12, 830–31.]

Rose and his co-workers determined antistreptolysin titers in the blood of 45 soldiers suffering from recurrent lymphangitis associated with filariasis contracted in the South Pacific. The titers were within normal limits in 39 of the 45 cases. The attacks of lymphangitis in these soldiers appeared to be due to allergic reactions to the parasitic infection ; secondary streptococcic infections were of little or no consequence as an etiologic factor.

WILLCOX, R. R. **Genital Oedema in relation to Filariasis in the Gold Coast.** *Brit. J. Venereal Dis.* 1945, Dec., v. 21, No. 4, 178–9.

Oedema of the external genital organs was present in 10 out of 875 African soldiers admitted to a hospital at Accra, Gold Coast, between June and September, 1944. Examination of the blood showed microfilariae of *Loa loa* in 5 and microfilariae of *Acanthocheilonema perstans* in 1 ; microfilariae of *Onchocerca volvulus* were found in the skin of 1 man who had also a guineaworm in the scrotum. Some of the 10 men gave a history of having had several attacks of genital oedema.

Treatment was by means of a suspensory bandage and in 4 cases the swelling subsided within a week ; one was operated on for elephantiasis of the penis and scrotum. [The incidence of filarial infection among the other 775 soldiers is not given.] *J. F. Corson.*

BONNET, R. Réflexions sur un cas de méningite aiguë à *Microfilaria loa.* [**A Case of Acute Meningitis due to the Microfilaria of** *L. loa.*] *Méd. Trop.* Marseilles. 1943, July–Aug., v. 3, No. 4, 273–7.

WANSON, M. & HENRARD, C. Habitat et comportement larvaire du *Simulium damnosum* Theobald. [**Habitat and Larval Development of** *S. damnosum.*] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 113–21.

This gives a detailed account of the ecology of *Simulium damnosum* in the neighbourhood of Léopoldville in the Belgian Congo. The biting of these

insects constitutes a serious nuisance during the months of September to January (*i.e.* the start of the hot season) ; *S. damnosum* is also the vector of *Onchocerca volvulus*.

The adult females migrate to the town from the rapidly running sections of the river by the way of shaded water-courses. They commonly migrate for several miles (45 miles is quoted as a maximum). Breeding goes on in various locations in the rivers, the larvae and pupae being attached to stones, submerged plants and wicker-work fish traps. A sudden change in water level causes a high mortality, but a gradual rise or fall allows the larvae to migrate to a suitable situation. The life-cycle from egg to adult takes about nine days, and the adult female lives about three weeks. In certain regions *S. damnosum* is frequently parasitized by microsporidia ; this causes a substantial mortality.

Kenneth Mellanby.

Wanson, M., Henrard, C. & Peel, E. *Onchocerca volvulus* Leuckart. Indices d'infection des simulies agressives pour l'homme. Cycle de développement chez *Simulium damnosum* Theobald. [*O. volvulus* ; **Indices of Infection of** *Simulium* **and Cycle of Development.**] *Rec. Travaux Sci. Méd. Congo Belge.* 1945, July, No. 4, 122–38, 8 figs. on 1 pl.

Simulium damnosum and *S. albivirgulatum* both attack man in the Belgian Congo, but only *S. damnosum* is of importance as a vector of *Onchocerca volvulus*. The population of fishermen living near the rivers in which the vector insects breed is heavily infected (up to nearly 100 per cent.), and 15 per cent. of *S. damnosum* captured from their villages were infected. In villages five miles away from the breeding sites, 65 per cent. of the people and 3 per cent. of the *Simulium* were infected. Further afield the infection rate in both man and insects declined still more.

Adults of *S. damnosum* have been kept alive in the laboratory for over a week in sufficient numbers to demonstrate the whole cycle of *O. volvulus*, which takes six or seven days. *Kenneth Mellanby.*

Nettel F., R. Contribución al estudio de la distribución de los simulidos en el estado de Chiapas. [**The Distribution of Simulidae in the State of Chiapas.**] *Medicina.* Mexico. 1945, Nov. 10, v. 25, No. 495, 455–9, 1 fig. English summary.

" 13,505 simulids were collected in 256 localities in the south of the State of Chiapas, where onchocerciasis prevails. In the mountainous regions the captures were made on man and near the coast on animals. In places where onchocerciasis is more prevalent, *Simulium ochraceum* was found in greatest proportion, being followed by *S. metallicum* and *S. callidum*. The other species were collected in small numbers, not constituting a plague like the former."

Clapham, Phyllis A. **On some Characters of the Genus** *Trichuris* **and a Description of** *T. parvispicularis* **n. sp. from a Cane Rat.** *J. Helminthology.* 1945, v. 21, Nos. 2/3, 85–9, 13 figs.

Schüffner, W. Die Bedeutung der Staubinfektion für die Oxyuriasis. Richtlinien der Therapie und Prophylaxe. [**The Importance of Dust-borne Infection in Enterobiasis. Rules for Therapy and Prophylaxis.**] *Münch. med. Woch.* 1944, Aug. 11, v. 91, Nos. 31/32, 411–14. [Numerous refs.]

Infestation experiments on seven persons (doctors and students) enabled Schüffner and Swellengrebel to show that eggs of *Enterobius* which had dried for three days and longer in room dust retained their full

powers of development. Six out of the 8 subjects passed worms after 36 to 53 days; that is to say, the shortest time required before worms were passed was 36 days and the longest 53 days. Thus dust-borne eggs are a source of infestation [*cf.* also CRAM, this *Bulletin*, 1943, v. 40, 618].

The large numbers of eggs found by Schüffner and Swellengrebel [this *Bulletin*, 1945, v. 42, 924] in the dust of a school dining hall leaves no doubt of the importance of this source of infestation.

Eggs may get into the dust in various ways. LEUCKART thought that the eggs dry with the faeces, because the female worms lay their eggs on the outer surface of the faeces; but it is doubtful whether these eggs play any part in the distribution of the worms. Most of the faeces are deposited in the closet and do not dry. The eggs in the very small amount of faeces deposited in the outer world are so much diluted by the atmosphere that hardly one of them will find a host. The main source of eggs in dust is the anal region, which is also the main source of finger infection. From the anal region eggs pass into the air, not singly, but in clusters.

Many eggs which pass into the unenclosed atmosphere are lost or fail to develop; but within enclosed spaces the air can carry a wide variation of numbers of eggs. In one school studied by the author the number of eggs found on about 10 sq. decimetres (q.d.m.) [roughly 1 sq. foot] of surface was 119 in a large dining hall, 305 in classrooms and about 5,000 in the much smaller closets. The size of the room is not the only factor which affects the density of eggs found. SMALT (*Nederl. Tijdschr. v. Geneesk.*, 1944, p. 20) found that the egg content in female closets was greater, although the worm infestation of the females was not higher than that of the males. Doubtless dissemination of eggs is favoured by the movements of female clothes.

The spaces just mentioned are, however, used only for a short time. There is a much smaller air space which is used for half the life of the infested person namely, the air space under the bed clothes. This has been studied by OLÉNIKOFF (*Russ. J. Tropenmed. u. med. u. vet. Parasitenk*, 1929, p. 393). This space is an important source of dust-borne infestation, for the eggs are disseminated night after night by the movements of the sleeper and can often enter the nose and mouth in considerable numbers. This is especially a risk for males, who tend to draw the bedclothes over their heads more often than females do and this may explain why males, in spite of all precautions and repeated drug treatment, are not freed from their infestations. Eggs are also distributed from the bed into the air by bedmaking.

Dust-borne infection plays an important part in the epidemiology of enterobiasis. It does not cause heavy infestations, which arise from finger infestations only, but it introduces enough eggs to cause repeated light infestations. Finger infection may be added to it and then severe enterobiasis may arise. It is important to differentiate between these two kinds of infestation. The hypothesis of an "enterogenous" development of *Enterobius* within the alimentary canal has been suggested to explain repeated infestations and failures to cure, but dust-borne infestation can explain these more simply and equally well.

Schüffner's own experiments show that, in all the persons studied by him, the infestations, which lasted 12 to 27 days, ceased without treatment. The same result appears to have been obtained in the twelve experimental infestations with fresh eggs recorded in the literature [no refs. are given], although this was not always explicitly stated. In one person only, experimentally studied by v. DRIGALSKI and KOCH, (*Deut. med. Woch.*, 1925, p. 309) did the infestation reappear after nine months, in spite of every care. In this instance dust-borne infection was responsible for the reappearance of the infestation. Without it *Enterobius* dies out. In the author's experience, its length of life is 37 to 93 days.

Preventive measures should be based upon a distinction between management of the individual suffering from active enterobiasis, and general measures directed against carriers, who exhibit inactive (latent) enterobiasis (see HAMBURGER, *Münch. med. Woch.*, 1943, p. 723). For latent enterobiasis there is no treatment; hygiene thereby acknowledges its weakness; we can only try to limit the degree of the infestation. In active enterobiasis the intensity of the irritation may vary not only with the number and vigour of the worms, but also with the sensitivity of the subject; some subjects who are not "ticklish" may suffer little from even an active enterobiasis (*e.g.*, one of the persons used experimentally by Schüffner). In active enterobiasis also dust-borne infestation is of capital importance. It has hitherto been much underestimated; it provides a gap in the control plan which is responsible for failures in treatment. It is useless to enforce severe hygienic rules if dust-borne infestation is not also controlled. The rule is to treat the symptoms only and to do this by the simplest means. Schüffner recommends for this purpose small enemas (*Einläufe*) of 30 to 50 cc. of water for the temporary appeasement of the anal irritation. These wash out the worms in the anal area. Inspection of the rectum at the height of the irritation shows active worms in the anal folds. When these are removed the irritation ceases at once. The view of LORENZ (*Med. Klin.*, 1925, p. 95) that the irritation is due to larvae of *Enterobius* is not correct, because the larvae are too small and Schüffner saw them hatch in the anal region only very exceptionally. Schüffner agrees that some larvae may hatch here and creep back to continue their development in the intestine, as LANGHANS (*Arch. Kinderhk*, 1926, v. 77, 27) suggested, but he has, as yet, not enough evidence to prove it; this is, at any rate, not true enterogenous development, but merely avoidance of the usual entry by the mouth.

Small enemas are, in Schüffner's experience, sufficient to remove the worms present in light infestations; often there is only one worm present. High enemas given with the object of getting at the immature worms higher up in the intestine are not only quite superfluous, but are also often very disturbing to the subject. These worms are better eliminated by anthelmintics. No known substance has all the properties of an ideal anthelmintic. The author discusses and apparently recommends gentian violet [see also CRAM, this *Bulletin*, 1943, v. 40, 618]. Danish use of this drug is similar to its use by American workers. Reckoning the life of *Enterobius* as from 37 to 53 days (see above), Schüffner concludes that if eggs appear in less than 37 days after anthelmintic treatment (or, adopting LENTZE's (*Zent. f. Bakt.*, 1935, v. 135, 156) estimate of the length of the life history, in less than 25 days), the anthelmintic has failed. If eggs appear between 37 and 53 days after treatment the drug may have eliminated the worms present, but a new infestation (*e.g.*, a dust-borne one) may have occurred. If eggs appear after the 54th day after treatment, a new infestation must have occurred, even if the drug has eliminated all the worms originally present.

Known anthelmintics, however, must not be expected to give a permanent cure, because dust-borne infestation is so difficult to control. The author deprecates the use of aperients, which are, he thinks, practically never justified. For prophylaxis against finger infection, Schüffner recommends increased cleanliness of the hands and washing of the anal region immediately after rising in the morning. This gets rid of eggs before the daytime clothes are put on and the child remains all day in a personal environment more or less free from eggs. Washing after each stool does some good but does nothing directly against the worm. The practice of it is based on the faulty observation that eggs are laid in the intestine and are taken up only from the stool. Schüffner and Swellengrebel found, on the contrary, that eggs are laid only very exceptionally in the intestine.

The wearing of closely-fitting bathing drawers at night is a useful means of prevention of soiling of the hands, although eggs, as LENTZE [this *Bulletin*, 1936, v. 33, 121] showed, can easily pass through the most closely woven materials. The drawers prevent, however, the picking up of eggs by scratching and this justifies their use; they can convert an active into a latent enterobiasis and they hinder distribution of eggs in the bed and thus prevent dust-borne infestation under the bedclothes. Loose night clothes help this kind of infestation.

The precautions so far mentioned may practically close the finger-mouth route of infection, but they only partly restrict dust-borne infection, which is especially important at night in bed. KOCH, LENTZE and others think that *Enterobius* ceases to migrate out from the anus after midnight, so that a second washing of the anal region after midnight may do good; this is, however, troublesome for the mother and may, for that reason alone, not be justified. Another measure is to close the anus with suppositories, ointments, etc. This together with the wash immediately after rising in the morning will almost completely prevent dust-borne infection.

The author thinks that many textbook measures are unnecessary: they may also lead to threadworm neurosis. Among these he includes treatment of the members of the family suffering from latent enterobiasis, daily changes of bedclothes and underclothes and sterilization of these, keeping the nails short, change of diet, stool examinations, high enemas and purges. Dust-borne infection cannot be entirely eliminated, so that it is useless to aim at permanent cure by such strict rules. The author is discussing enterobiasis in Amsterdam, where he says that 100 per cent. of children are infested. When dust-borne infection is not a risk, the author recommends the simple measures given above, because in 5 to 7 weeks the worms will naturally die out. *G. Lapage.*

GAASE, A. Ueber die Verwendbarkeit der Komplementbindungsreaktion zum Nachweis der Trichinose. [**On the Value of the Complement-Fixation Reaction for the Diagnosis of Trichiniasis.**] *Münch. med. Woch.* 1944, Aug. 25, v. 91, Nos. 33/34, 440–41. [14 refs.]

The occurrence of a localized outbreak of trichiniasis in Germany in 1943 enabled the author to test further the value of the complement-fixation reaction tested by him and others in earlier work. The illness was not severe and *Trichinella* could not be found by meat inspection. The symptoms were more subjective than objective. Within seven weeks the sera of 110 members of the Wehrmacht were sent to Gaase to be tested for trichiniasis. Of these, 82 (74·5 per cent.) were feebly or strongly positive. This percentage of positives seemed to be low, but only one sample of 17 out of the 28 negative sera was sent for examination, so that probability of a positive reaction was not great. It was, therefore, all the more striking that in some subjects the reaction was positive shortly after the appearance of the symptoms [the author does not say how long after]. The limited amount of antigen available prevented the use of daily tests to detect the earliest time when positive reactions appeared, but it can be said that the number of positives would have been higher if this point could have been systematically investigated. The value of the complement-fixation reaction for the diagnosis of early cases of light *Trichinella* infestations was, however, demonstrated. In three subjects the reaction was positive or lightly positive on the second day, which is an earlier date than that observed by Gaase in experiments on animals. By the seventh day the number of positives reached 13, the first strongly positive reaction occurring on the fourth day. The author does not, however, claim any finality for these figures. He used an antigen prepared from swine.

Eosinophilia is an almost constant symptom of trichiniasis, but the degree of it does not indicate the degree of the infestation; nor does the degree of prevention of haemolysis in the complement fixation reaction indicate the severity of the *Trichinella* infestation. For these reasons the author enquired whether there is any relationship between the eosinophilia and the antibody content of the subject's blood. No such relationship could be found. In most subjects with a strongly positive complement fixation reaction the number of eosinophils was markedly increased, but some giving lightly positive reactions had 30 to 40 per cent. of eosinophils and, conversely, others giving strongly positive reactions had 0 to 7 per cent. of eosinophils. There is little evidence to decide whether the eosinophilia or the complement-fixation reaction is the more reliable for early diagnosis. Experimental work on animals has enabled the author to demonstrate by means of the complement fixation reaction the presence of a *Trichinella* toxin in the brain [see this *Bulletin*, 1945, v. 42, 481 and the literature there quoted].

The successful use of the complement-fixation reaction for the detection of light infestations of man with *Trichinella* suggests that similar light infestations occur in animals. This consideration, together with the fact that outbreaks of trichiniasis occur in areas in which careful inspection of meat for *Trichinella* has failed to detect it, seems to justify the supplementing of meat inspection with complement-fixation reactions done upon the swine. *G. Lapage.*

DEFICIENCY DISEASES.

GILLMAN, T. & GILLMAN, J. **Hepatic Damage in Infantile Pellagra and its Response to Vitamin, Liver and Dried Stomach Therapy as determined by Repeated Liver Biopsies.** *J. Amer. Med. Ass.* 1945, Sept. 1, v. 129, No. 1, 12–19, 8 figs. [Refs. in footnotes.]

In this paper the authors describe in detail the damage found in liver biopsy specimens (taken according to a modification of the technique of Iversen and Roholm [see this *Bulletin*, 1945, v. 42, 1046]) from African children suffering from the type of infantile pellagra which is so severe that 50 per cent. of them die though treated with vitamins and a satisfactory diet. The condition found, and the clinical signs, together with details of the authors' new and successful treatment with a dried stomach preparation, are referred to in previous papers abstracted in this *Bulletin*, 1944, v. 41, 1057; 1945, v. 42, 748; 1946, v. 43, 59.

The present communication is based on a study of 20 livers. From the pathological point of view these fall into three categories. In the first there is enormous accumulation of fat in the liver cells, in the form of single, large, pale-staining globules filling the entire cell. In the second (less serious) form almost all cells contain multiple coarse droplets of fat. In the third the cells contained dust-like particles of fat.

The authors discuss the results of treatment, again emphasizing the value of dried stomach, even in the restricted amounts they were able to give. They think that the presence of large amounts of fat in the liver and in the stools, though the diet of the patients had previously consisted largely of carbohydrate, and though there was little fat elsewhere, indicates that carbohydrate is converted in the body to fat, but that utilization of the fat is deficient, and that it is excreted into the bowel or deposited in the liver cells. Vitamin treatment may not only be useless, it may actually be harmful, and it is known that large doses of nicotinamide produce fatty infiltration in the livers of rats. Other workers have noted the beneficial action of liver therapy in pellagra, but in

comparison with the authors' results with dried stomach, the action of liver is slow and incomplete. They stress again their opinion that dietary imbalance may initiate the disease, producing secondary changes which are not susceptible of cure by administration of vitamins.

The African, in the Johannesburg area from which the authors write, exists in poor economic conditions, and his liver is subject to repeated insults of this kind; it is likely that the known high incidence of cirrhosis and of primary hepatic carcinoma are due in no small measure to this chronic malnutrition.

Charles Wilcocks.

SPRUE.

MAEGRAITH, B. G., ADAMS, A. R. D., HAVARD, R. E., KING, J. D. & MILLET, R. F. **Carbohydrate Absorption in Sprue.** *Lancet.* 1945, Nov. 17, 635, 2 figs.

In the course of experimental observations on cases of sprue the authors investigated the absorption of glucose and fructose; the former is absorbed from the small intestine mainly after phosphorylation [" the process of introducing the trivalent PO group into an organic molecule " *Dorland's Med. Dict.*] while fructose is absorbed chiefly by simple diffusion through the intestinal mucous membrane.

After each patient had taken 100 gm. of sucrose by mouth the glucose and fructose levels in the blood were estimated every half-hour for 2½ hours. In the active cases of sprue the glucose curve was flat, the maximum rise seldom exceeding 20 mgm. per 100 cc. above the fasting level; the absorption was " of the same order as that of fructose." The fructose absorption curve was always within normal limits. Hence in these cases of active sprue the absorption of glucose was much reduced, while that of fructose was unaffected. The reduction of glucose absorption is considered to be due to failure of phosphorylation in the small intestine.

Certain substances are known to be able to inhibit phosphorylation in the small intestine, and magnesium, *in vitro*, " plays an important part in phosphorylation." The authors therefore estimated the plasma levels of Ca and Mg in their patients; the Ca levels showed little difference from the normal, but the Mg level was low in two patients (0·75 mgm. and 1·2 mgm. per 100 cc., respectively) who were acutely ill and had tetany at the time. In these two patients no direct relationship between the recovery of the carbohydrate absorption and the return of the Mg levels to normal was observed. In other acute cases without tetany a low Mg level was not found. *J. F. Corson.*

SINGH, B. **Fatty Diarrhoea. A Report on 26 Cases.** *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8, 388–90.

The patients, chiefly non-vegetarian Muslims, were admitted to a malnutrition ward in an Indian military hospital after periods ranging from 4 to 36 months (the majority within one year) in the forward areas.

The severity of their complaints could be classified into severe, moderately severe, and mild. The manifestations essentially consisted of looseness of the bowel (3 to 13 motions in 24 hours), griping pains, vomiting and retching after meals, weakness and wasting, and, in a few cases, " feverishness ". The stools were pale, copious, of porridge-like consistency and slighty frothy, and contained 50 per cent. of fat, the ratio of split to unsplit fat being about normal.

All the men complained of soreness of the tongue at some time during their stay in hospital. Their red cell counts and haemoglobin content were not grossly abnormal ; in 9 cases where a fractional test meal was done, it revealed hypoacidity or achlorhydria.

The treatment included attention to diet and administration of drugs, including dilute hydrochloric acid, nicotinic acid, and the sulphanilamide drugs ; the latter controlled the diarrhoea while they were being taken, but it recurred on their cessation if the general condition of the patient had not materially improved. Small repeated blood transfusions were given in a few cases, without obvious benefit.

The author attributes the condition to restriction in food intake added to debilitation consequent on dysentery ; a vicious circle thus being set up. The sulphonamides were of benefit in breaking the circle and restoring a more normal equilibrium from the sprue-like state (" para-sprue ") into which the cases had declined. *A. R. D. Adams.*

HERNÁNDEZ MORALES, F. **Gastroscopic and Rectosigmoidoscopic Observations in Tropical Sprue.** *Puerto Rico J. Pub. Health & Trop. Med.* 1944, Dec., v. 20, No. 2, 257–67. [Refs. in footnotes.] [Spanish version 268–79.]

Sixty-one gastroscopic examinations were performed on 36 sprue patients, during the acute diarrhoeic stage, and after liver extract treatment had been given for varying periods. In 55 per cent. atrophic changes were observed in the gastric mucosa. Practically all showed acute glossitis with absence of the papillae, though, following liver treatment, the tongue showed great improvement. Sixteen were examined after treatment, and in 10 the appearance of the gastric mucosa was restored to normal.

Recto-sigmoidoscopic examinations undertaken during the acute diarrhoeic stages revealed several types of lesions, such as atrophic patches, oedema, friability, purpuric spots and superficial inflammation.

Gastroscopic examination in sprue is the only available method of studying the changes in the gastric mucosa in this disease. It is once more stated, in confirmation of the views of OLLEROS (*Puerto Rico J. Pub. Health & Trop. Med.*, 1938, v. 13, 503) that the atrophy of the gastric mucosa is more intensive in pernicious anaemia than in sprue. *P. Manson-Bahr.*

RODRIGUEZ-MOLINA, R. **Sprue in Puerto Rico—Ten Years Later.** *Puerto Rico J. Pub. Health & Trop. Med.* 1943, Mar., v. 18, No. 3, 314–40. [Spanish version 341–63.]

For the purposes of this study the sprue syndrome is held to be a chronic deficiency state characterized by its insidious onset, chronicity of symptoms, progressive development of gastro-intestinal disturbances—mainly dyspepsia, soreness of the tongue and mouth, meteorism and diarrhoea. The stools are usually liquid, foamy, greyish, foul smelling, voluminous and fatty. Stomatoglossitis, atrophic gastritis, and recto-sigmoiditis are important findings. A macrocytic hyperchromic type of anaemia with a megaloblastic marrow accompanies about 90 per cent. of the cases. Loss of weight occurs in the same percentage of cases ; fever in about 40 per cent.

The symptoms of sprue may appear and become fully developed in the course of a few weeks, but more usually a few months, as the chronicity of symptoms is typical ; this symptom complex may continue, if untreated, for several years before death ensues. Relapses are common, but spontaneous remission of gastrointestinal symptoms or of the anaemia are rare.

The rapid loss of weight and strength is associated with intestinal hypermotility, with resulting malabsorption, and chronic and progressive starvation. Derangement of the metabolism of fats, carbohydrates and proteins is closely related to the failure of the absorptive intestinal function, and is believed to be intimately linked with the clinical picture of the syndrome.

This deficiency state in sprue is amenable to replacement therapy, and symptoms can be cured by liver extract. The group studied comprised 51 males and 49 females, ranging from 12 to 78 years of age, the mean age for the group being 40·14 years. There were 87 white and 13 coloured individuals; among the latter were two full-blooded negroes, the others being mulattoes. Ninety-eight persons were natives of Porto Rico. With few exceptions the individuals were indigent and, when first examined, presented the fully developed picture of the sprue syndrome. The liver extract employed for intramuscular injection was prepared according to instructions given by W. B. CASTLE. This is a crude, unconcentrated product from 343 Liver Powder Lilly, and its efficacy for sprue and other macrocytic anaemias had been demonstrated. One cc. of this extract was equivalent to about 5 gm. of fresh liver. In the out-patient department it was given intramuscularly in doses of 5 to 10 cc., usually 5 cc. three times a week. Injections of 5, 8 and 10 cc. were often given daily in the wards. One individual received as much as 20 cc. *intravenously* daily. Whenever possible, reticulocytes were counted daily during the first two weeks of liver therapy. Wintrobe's haematocrit was employed to determine the volume of packed cells, and a Newcomer-Klett haemoglobinometer to estimate the haemoglobin in grammes and percentages. The diet prescribed, that of Ashford, was of low residue, high protein, low fat and low carbohydrate, which assured assimilation even in presence of diarrhoea. In practice it included certain Island carbohydrate foods, such as plantains, bananas, *yautias* (a tuber, similar to potato). The diets supplied from 1,500 to 2,000 calories per day.

Of the drugs taken orally the chief was a digestant of hydrochloric acid and pepsin, and a small amount of strychnine. Another preparation contained tincture of opium, prepared chalk and bismuth subcarbonate used for stubborn diarrhoea.

A table has been compiled of the number of deaths from sprue per 100,000 of population in Porto Rico during the decennial period 1928 to 1938. For the purposes of comparison, deaths from other anaemias are also shown. In 1928 there were reported 88 deaths from sprue with a rate of 5·9 per 100,000; in 1938 the total number of deaths reached 103 and the rate 5·8 per 100,000. In white individuals, the age groups showing the greatest number affected were 20–29 for females, 20–29 and 40–49 for males. Twenty-six white males, or one-half of the male group, were affected between the ages of 20 and 50. There were 11 white women in the 20–29 group, a higher number than in any other. This is significant as indicating that sprue attacked women most often during the period when pregnancy was most likely to occur and that its onset occurred, not during pregnancy, but after delivery. In the coloured group the largest number of females (3) fell in the 20–29 group; of the 6 males there were two in each of the three groups between ages 20 and 50.

A total of 75 white and coloured individuals were discharged as improved and did not return during the ten-year period 1931–1941. The average duration of treatment was three years, with a range of one month to ten years, and the average hospital sojourn for 27 cases was 40 days.

The number of relapses was generally less in patients below 40 years of age. Upper respiratory infections were responsible for the greatest number of relapses; next in order were dietary indiscretions. Cessation of liver therapy was also a cause.

The earliest indication of improvement under liver therapy was rapid and progressive disappearance of the lingual and buccal lesions, accompanied by change in the appearance of mouth lesions. On diet treatment alone, however, this process was delayed for several weeks, nor were all the papillae completely regenerated. The return of the long-lost appetite was taken as an early indication of improvement. Relief of gastrointestinal symptoms was not apparent until a later date. It is believed that improvement was more rapid under liver and diet than with liver alone; under combined liver and diet therapy the number of bowel movements might diminish as early as the second or third week. It was observed that any indiscretion in the diet, even in those who were symptom-free, always resulted in a change in the appearance and frequency of the stools.

A rise in reticulocytes may be taken to mark the earliest indication of blood regeneration following liver therapy. The peak of this increase usually occurred from the fifth to twelfth day. When the red cells were more than three million, the reticulocyte count was rarely higher than 10 per cent. As a rule, the proportion of reticulocytes became normal (1 to 2 per cent.) by the end of the second week. In general, the reticulocyte peaks were lower in sprue than in pernicious anaemia. Changes in the morphology of the red cells, such as anisocytosis, and poikilocytosis, were greatly diminished during the first few weeks of treatment, but might persist for months, particularly when macrocytosis was present.

In about 50 per cent. of cases the mean corpuscular volume rose shortly after administration of liver extract, as the amount of cells and their packed volume increased.

The leucocyte count, if low, usually returned to normal between the fourth and fifth weeks of treatment, and the differential count also returned to normal. Macrocytosis of leucocytes disappeared promptly in the majority of cases. Low platelet counts returned to normal, but not before the third or fourth weeks of treatment.

The amount of liver extract required to maintain a person with a high threshold requirement in good health, once a full remission of symptoms had occurred, varied widely with different individuals. The erythrocyte and haemoglobin responded rapidly, " but normal or subnormal levels were maintained for longer periods in individuals below forty years . . . than in those over this age." In the older age groups clinical improvement, with disappearance of gastrointestinal symptoms, was frequently observed in association with subnormal blood levels.

The opportunity for observing permanent cures in sprue is lacking. It is known that of the 75 individuals discharged as improved, 65 have apparently remained well after five years without treatment.

Liver extract was given to one individual daily by the intravenous route in 10 and 20 cc. doses. No reaction, save pyrexia of 103°F., resulted, but clinical and haematological improvement was no more effective, nor did it appear any sooner, than when liver was administered intramuscularly.

P. Manson-Bahr.

Rodriguez Molina, R. **Sprue in Puerto Rico. A Clinical Study of 100 Cases.** *Puerto Rico J. Pub. Health & Trop. Med.* 1941, Dec., v. 17, No. 2, 134–51, 2 figs. [Spanish version 152–68.]

HAEMATOLOGY.

BERG, W. N. **Blood Cell Counts : their Statistical Interpretation.** *Amer. Rev. Tuberculosis.* 1945, Sept., v. 52, No. 3, 179–220, 12 charts. [28 refs.]

The main purpose of this very heavy and careful piece of work, which was undertaken for the Committee on Evaluation of Laboratory Procedures, is to describe the statistical aspects of blood cell counting so that any worker can make his own tests of significance by reading the tables provided. Taking as an example the red cell count, the author first shows the variability that may occur by chance in making repeated counts of a single dilution of blood. For instance, if 1,000 correct counts were made, each on 80 squares, and the mean number of red cells were 300, the individual counts would vary between 248 and 352. This variability is due to " chance " or " purely accidental " variations in the way the red cells stream across the squares in the chamber. The majority of the counts would lie in a narrower range, two-thirds, approximately, being between 283 and 317, but wider deviations will inevitably occur with some frequency. In practice this variation will be increased by variations in chamber size and in dilution pipettes. Thus the range of observed counts round the mean of 300 will be increased under normal conditions of careful routine from the 248 to 352 (above) to 224 to 376, two-thirds, approximately, lying between 275 and 325. The author briefly tabulates the frequencies with which counts would be expected to occur in this way round mean values from 200 to 800, and such statistical expectations have been found to be in accordance with observations.

The first problem arising, then, is to decide what information is obtainable from a single red cell count. Given, for instance, a count of 464 on 80 squares, this result could come from a patient with only 372 or as many as 600 cells, though most infrequently in either case. It might well arise from a patient with a real count lying anywhere between 400 and 540, a wide range. The table provided shows the possible limits for different observed counts.

The second problem concerns the method to adopt in determining that a single chamber count has been made correctly. One such method is to count the cells separately in each of five groups of sixteen squares, note the largest difference that occurs between any two of these five totals and from the table provided see whether such a difference is likely or unlikely to have occurred by chance. If the difference is unlikely, error should be suspected. A second method is to compare the actual with the theoretical Poisson distribution, but this is laborious in practice.

The third problem is to determine how large a difference between two consecutive red cell counts on the same blood may be due to random sampling. A table of ranges is provided to show the extent to which two such readings may be expected to vary by chance. Alternatively, from another table the ratio of the difference between the two counts to the standard deviation may be calculated ; if the difference is greater than three times the standard deviation the probability that both counts were correctly obtained on the same blood is very small. Using this method, the author gives clear examples of its application in three situations :—(*a*) counts on the same dilution ; (*b*) counts of different dilutions of the same puncture ; (*c*) counts derived from two punctures.

The fourth problem is whether two counts are better than one. If the first count happens to be close to the true value, chance will place the second count further away, making their mean a poorer estimate than the first count alone. Conversely, if the first count is far from the truth chance will place the second count nearer and the mean will in this case give a better estimate. Since the investigator cannot tell which situation he is facing, the mean of two counts

cannot be depended upon to furnish a better estimate than either one alone. For practically all other purposes, two counts are better than one.

A similar treatment and discussion is given to white cell counts and the neutrophil count, the latter being applicable to other differential counts so long as they exceed 5 per cent. of the total count. A table is given for estimating the amount of variation that may occur by chance for differential counts in which the observed percentage is less than 5.

[It is not possible in an abstract to reproduce the tables and explanatory matter in this paper, which should be consulted in the original.]

A. Bradford Hill.

ENGLISH, R. B. **Sicklaemia occurring in Africans in Northern Rhodesia.** *South African Med. J.* 1945, Nov. 24, v. 19, No. 22, 431.

"Sicklaemia is present in 17·52 per cent. of African males employed on the copper belt of Northern Rhodesia. No significant difference in the incidence among healthy and unhealthy subjects is noted."

ROBINSON, G. **A Rapid Method for detecting the Sickle Cell Trait.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1945, Dec., v. 39, No. 3, 264.

The "ferment broth" used by NEUDA and ROSEN [this *Bulletin*, 1945, v. 42, 825] in their rapid method for diagnosing sickle-cell disease, is really a mixed culture of intestinal organisms. The author has used broth cultures of various bacteria—*Pseudomonas fluorescens*, *Bact. coli*, *Staph. aureus*, *B. subtilis*—for the rapid production of sickling of the erythrocytes. The presence of living bacteria is necessary, as heating the cultures at 60°C. for 1 hour, filtering through Seitz Disk EK/3 or Pasteur-Chamberland Candle L3, or killing the bacteria with alcohol, produces inactivity, while suspensions from an agar culture are active without further incubation. "*Method.*—A drop of a 24- or 48-hour-old culture, previously tested for its activity against known sickling corpuscles, is placed on a slide, and a smaller drop of finger blood mixed with it, covered with a cover glass and examined under the microscope. In cases with the trait, or with active sickle cell anaemia, sickling of the corpuscles begins to show in from 1 to 5 minutes; in most cases 70 to 90 per cent. of the corpuscles being sickled in 15 minutes."

J. F. Corson.

WINSOR, T. & BURCH, G. E. **Sickle Cell Anemia, "A Great Masquerader" easily recognizable with Routine Use of Diagnostic Parameter.** *J. Amer. Med. Ass.* 1945, Nov. 17, v. 129, No. 12, 793–6, 4 charts.

Since sickle cell anaemia is such a great imitator, and because it may remain so subtle, it is necessary as a routine to study the blood for sickle cell anaemia in all negro patients. This can conveniently be done by the routine diagnostic use of the parameter [described by WINSOR & BURCH, see this *Bulletin*, 1945, v. 42, 484]; such a search in 612 consecutive negro patients showed 27 (4·4 per cent.) to have sickle cell anaemia. Two methods may be used in performing the test, one employing CO_2 (diagnostic parameter Δ_1) and the other venous stasis (diagnostic parameter Δ_2) to produce retardation of the rate of the erythrocyte sedimentation.

In the second method a sphygmomanometer cuff is applied to the arm and a pressure between the systolic and diastolic blood pressure is sustained for 6 minutes, after which 10 cc. of venous blood are withdrawn into a tube containing either citrate or oxalate crystals. A portion of this blood is then immediately placed in a Wintrobe sedimentation tube and the sedimentation rate

determined. The remaining portion of the blood is adequately aerated until it is bright red, by rotation at 2-minute intervals for 15 minutes in an Ehrlenmeyer flask, after which its sedimentation rate is determined. The diagnostic parameter Δ_2 is indicative of sickle cell anaemia when the difference between the sedimentation rates (uncorrected) is greater than 20 mm. per hour. If the difference is less than 20 mm. per hour the chances are 10,000 to 1 against sickle cell anaemia, and if the difference is greater than 20 mm. per hour the chances are 98 in 100 that the patient has sickle cell anaemia.

In the first method 5 to 10 cc. of venous blood are withdrawn into a tube containing citrate or oxalate crystals. A few cc. of this blood are then transferred to a rubber-stoppered Ehrlenmeyer flask into which pure CO_2 is introduced, and the flask is agitated at 2-minute intervals for 15 minutes or until the blood becomes dark blue. A few cc. of the original blood are similarly treated in an open flask and aerated for 15 minutes or until the blood becomes bright red. The sedimentation rates of the two samples are then compared immediately in a Wintrobe tube, and a difference greater than 27 mm. per hour between the rates is indicative of sickle cell anaemia.

In the study of 175 control patients with various diseases, including many types of anaemia, the average Δ_2 parameter was 5·3 mm. per hour, the extremes being 1 and 18 mm., while the average for 34 patients with sickle cell anaemia was 41·4 mm., the extremes being 29 and 65 mm. per hour. The average Δ_1 parameter for 437 control patients was 5·5 mm., the extremes being 0 and 24 mm. per hour, while the average for 73 patients with sickle cell anaemia was 53·5 mm., the extremes being 29 and 77 mm. per hour. Neither method gave a single false response. Sicklaemia, that is the sickle cell trait without anaemia, was not included in the series. A high concentration of CO_2 is necessary for a satisfactory result, and the gas used to saturate the blood with CO_2 in the second method should contain not less than 95 per cent. CO_2.

Experiments showed that the more severe the anaemia the greater was the tendency for the parameter to deviate from the normal. Significant differences in the haematocrit determinations of bloods treated with CO_2 and air occurred in patients with sickle cell anaemia. The increase in the haematocrit readings of patients suffering from sickle cell anaemia averaged 50·4 per cent., the extremes being 40 to 70 per cent., following treatment with CO_2, whereas in control patients the increase averaged 10·9 per cent. only, with extremes of 4·3 and 21·4 per cent. Unless the effect of CO_2 on the haematocrit reading is taken into consideration, grave errors may arise in the determination of the mean corpuscular volume and the mean corpuscular haemoglobin concentration in haematological studies of patients suffering from sickle cell anaemia, as careless collecting of blood may involve venous stasis. *F. Murgatroyd.*

VENOMS AND ANTIVENENES.

ROY. NAV. MED. BULL. 1945, No. 17, 40–46, 3 pls. (1 folding). **Poisonous Snakes.**

This is a concentrated account in simple language of the systematic position, habits and venoms of poisonous snakes of the world. Some of the statements made might be challenged, but on the whole the information supplied is not highly inaccurate. It is incorrect to state that " Many (vipers) have a dark inverted V on the back of the head." Again, the general statement that venom is " ejected through a canal in the fang " refers only to the Viperidae ; there is no mention of the grooved fangs of the Elapidae. Sound advice is

given on first-aid treatment of snake bite, with the exception of the recommendation that suction by the mouth should be carried out. There are several misprints in the table. For instance, the tiger snake is *Notechis scutatus*; the copperhead is *Denisonia superba*; the moccasin is *Ancistrodon piscivorus*; the spitting African cobra is *Naja nigricollis*. The statement in the table that *Naja nigricollis* is not very common is incorrect; it is, of course, one of the commonest poisonous snakes in West Africa. The drawings accompanying this article would have been better omitted.

B. G. Maegraith.

Freedberg, A. S. & Riseman, J. E. F. **Cobra Venom in the Treatment of Angina Pectoris.** *New England J. of Med.* 1945, Oct. 18, v. 233, No. 16, 462–6, 4 figs. [13 refs.]

A contribution of the highest interest. Cobra venom has been tried for relief of pain in many conditions—cancer, tabes, leprosy, neuralgia and others—and benefit has been noted, but always judged by the clinical history only, never objectively evaluated. It has been difficult to decide how much was due to the drug and how far the benefit was purely psychological, because the use of inert *placebos* often gave relief. Among the cases on record in the literature are 14 of angina pectoris.

The authors' study is based on 12 cases of angina pectoris from coronary arteriosclerosis, existent for periods ranging from 2 months to 7 years. The amount of work necessary, under standardized conditions, to bring on the pain was gauged by Riseman and Stern's method, their "standard exercise tolerance test." The patients were relegated to one of three groups: Group I reacting well to nitroglycerin and able, under its influence, to do double the work possible without the drug (4 patients); Group II able to do 50 per cent. more work after nitroglycerin (3); Group III giving no response to nitroglycerin or other usual methods of treatment (5). Seven out of the 12, four of them among the five of Group III, showed an improvement clinically and in standard exercise tolerance of the injection of cobra venom. The dosage at first was 1–2 cc. (10–20 mouse units, *i.e.* the m.l.d. for a 20 gm. mouse) daily injected into the deltoid, for 3–7 days, but the best dosage was found to be 1 cc. (10 mouse units) three times the first day, then once daily for 7 days. The injections caused local pain, but not severe enough to interrupt the course. Relief might last for some 5–6 weeks, or for a few days only after the course was completed, but the pain then returned and subsequent courses were less beneficial and, although the treatment might be continued, the pain would return and the standardized exercise tolerance fall to the original level. No toxic effects followed from the dosage stated above, but one patient who was given twice these doses on the first day suffered from pain in the chest, nausea, vomiting and diarrhoea of such severity as to call for cessation of the treatment. The important fact to be noted is that, though the pain may be relieved, the process underlying it—the pathological cause—remains unchanged and unaffected; the electrocardiogram after exercise is the same as that when no treatment is given; in other words, the action of the venom is not to cause dilatation of the coronary vessels. Also, as it takes some time—three days on an average—to bring about its effects, the venom would be useless for relief of an acute attack.

[The action in relieving pain without affecting the underlying pathological condition is closely analogous to relief of pain by hypnotic suggestion. The abstracter knows of the case of a man suffering from angina pectoris applying to a medically qualified hypnotist for relief. The latter refused, stating that the pain, which till then had not been very severe and was controlled by amyl

nitrite, was a warning to him not to hurry or over-exert himself. The patient applied to another hypnotist, not a medical man, who gave him relief and he found he could do more, such as quickening his pace to catch his morning train without pain. Soon after, he hurried thus a little more than usual and died of a heart attack on getting into the railway carriage. The pain had been relieved, but the underlying condition remained, of course, unaffected. This does not imply that the venom merely acts psychologically, for cobra venom is known to be an analgesic.] *H. Harold Scott.*

DERMATOLOGY AND FUNGUS DISEASES.

PETERS, J. T. **A Clinical Cure of Madura Foot.** *Amer. J. Trop. Med.* 1945, July, v. 25, No. 4, 363–5, 2 figs. [10 refs.]

Madura foot may be caused by any one of 13 species of *Actinomyces* or by any one of 19 species of true fungi (belonging to two classes and eight genera), yet the clinical picture is very similar in all cases; this suggests that there is some "common denominator", *e.g.*, the production of toxins with similar pathological effects on the tissues. In the U.S.A., the usual cause is a true fungus, *Monosporium apiospermum*, cases due to *Actinomyces* being much rarer; the present case is probably only the third case of Madura foot due to *Actinomyces* in the U.S.A. that has been confirmed by culture of the organism.

The patient, a coloured man aged 53, was admitted to the Charity Hospital, New Orleans, on January 3rd, 1944, with a swollen left foot, in which he said he felt occasional moderate pain. The swelling began in 1942, grew larger, and discharging sinuses appeared. X-rays showed decalcification of the bones with small punched-out areas at the bases of the 3rd and 4th metatarsals and at the distal end of the 4th metatarsal. What appeared to be *Actinomyces asteroides* (Eppinger-Gasperini) was isolated from the pus of the sinuses.

Treatment.—Penicillin was given for four weeks without effect, the total dosage being 1,050,000 units. Sodium propionate was next tried, as dressings containing 20 per cent. and as injections of isotonic solutions into the sinus tracts—also without effect. Iodides were not tried since they have always failed in Madura foot due to *Actinomyces*. Finally, sulphadiazine, 1 gm. every four hours in the daytime, was given for three weeks, the urine being examined daily and the blood twice a week. The blood levels during the day were always about 8 mgm. per cent. His slight fever disappeared after one week of this treatment. A culture of slow growth was obtained at the end of the three weeks' course but the patient refused further treatment, as the swelling had much decreased in size, and went home. He was advised to take methyl-sulphadiazine at home but did not do so for reasons of expense and for the same reason did not reappear for six months. His foot was then of normal size, the sinuses had all healed, and he was able to do all his work as a farm labourer. He was again seen after six months and was still apparently quite well. The author regards the case as a "clinical cure." *J. F. Corson.*

CARRIÓN, A. L. & KNOTT, J. **Mycetoma by *Monosporium apiospermum* in St. Croix, Virgin Islands.** *Puerto Rico J. Pub. Health & Trop. Med.* 1944, Sept., v. 20, No. 1, 84–99, 22 figs. on 7 pls. [Refs. in footnotes.] [Spanish version 100–107.]

"The first recognized case of maduromycosis in the Island of St. Croix, Virgin Islands, is herein studied and reported. The infection was of the white

grain type and its etiologic agent was a Hyphomycete, identified as *Monosporium apiospermum*, Saccardo 1911. Attention is called to certain morphologic peculiarities of this species, which should be taken into consideration for future classifications."

CATANEI, A. & KERVRAN, P. Nouvelle mycose humaine observée au Soudan français. [**A New Mycosis of Man found in French Soudan.**] *Arch. Inst. Pasteur d'Algérie.* 1945, Sept., v. 23, No. 3, 169–72.

The authors identified a case of histoplasmosis of an unusual type at Bamako in the French Sudan. The disease seems to have been localized in the right temporo-maxillary region, where it formed a suppurating granulomatous tumour about the size of a hen's egg attached to the ascending ramus of the mandible. An exploratory puncture released about 20 cc. of brownish-yellow, fluid pus containing the fungus in the form of thick-walled oval or rounded bodies having a longer diameter of 6, 12 or even 15 microns, some of which had an appearance of budding. In culture, the fungus developed the characteristic morphology of *Histoplasma capsulatum* in the mycelial form ; reference is not made to the development of the yeast form in culture. The lesion was cured by injecting 1 cc. of lipiodol, on two occasions, into the cavity left after evacuation of the pus. The culture was infective, apparently with little pathogenicity, for mice and guineapigs, but not for rabbits. In the pus of the artificially induced lesions the fungus was found chiefly in the form of small yeasts, 3·5 to 4·0 microns in diameter, with occasionally a larger form.

[The question whether the *Histoplasma* isolated from African cases of histoplasmosis is a different species from *H. capsulatum* Darling, 1906, is worth considering.] *J. T. Duncan.*

HEAT STROKE AND ALLIED CONDITIONS.

FARINAUD, M. E. L'homme et le climat colonial. [**The Influence of Tropical Climates on Man.**] *Méd. Trop.* Marseilles. 1944, May–June–July–Aug., v. 4, No. 3, 194–224, 1 folding chart.

In this review of the effects of tropical climates on man, the author has gathered his widely ranging material under two main headings, namely, the Physical Climatic Complex, and the Effect of Tropical Conditions on Organic Functions. The first includes the geographical and meteorological considerations required to explain tropical climatic characteristics and concludes with a series of climatograms for various areas in French Africa and Indo-China. These are built up on plots of mean monthly temperatures against mean monthly relative humidities at the different places. It is shown that the climatograms for most of the French possessions differ markedly from that of a typically temperate region inhabited by a white population, and both are removed from the zone of maximum comfort.

In the second part of the review the author attempts to indicate how far the human physiological constants of temperate regions are altered by tropical conditions. Changes in the blood pressure and the concentration and composition of blood, in basal metabolic rate, and in excretory activity of skin and kidney are briefly discussed, but, unfortunately, where investigators are named no references are given to their publications.

The conclusion reached is that climatic conditions alone may cause a transitory effect, but that so far they have not been shown to have any profound or lasting effect on the physiological functions discussed. This conclusion is also

applicable to the psychological state of the inhabitant of the tropics. The author observes that the inconveniences and annoyances of colonial life, often aggravated by excessive taking of alcohol or drugs, form the groundwork on which the neurasthenic and depressive states develop. He also stresses that the effect of the tropics on man can more adequately be considered as a "meteoropathological" problem, since many of the harmful effects imputed directly to the climate, are often the result of pathological changes due to parasitic infections. *A. F. Munro.*

RIEMERSCHMID, Gertrud. **Some Aspects on the Effect of Solar Radiation and other Factors of the Climatic Environment on Human Beings. B. Solar Radiation in South Africa and Europe and its Effect on the Human Body. C. The Ultra-Violet Solar Radiation. D. The Interrelationship between Quantity and Quality of the Ultra-Violet Solar Radiation and its Biological Effects.** *South African Med. J.* 1945, Aug. 25, Sept. 8 & 22, v. 19, Nos. 16, 17 & 18, 282–7 ; 308–10 ; 331–4, 19 figs. [27 refs.]

[An abstract of the first paper (Part A) was published in this *Bulletin*, 1945, v. 42, 317]. Part B in this series of papers on the biological effects of solar radiation on man is concerned with the heating effects of visible and infra-red radiations. Part C deals with the intensity and quality of ultra-violet radiation, and part D refers to the interrelation between quantity and quality of solar radiation and biological effects. The data discussed came mostly from the South African Solar Radiation Survey of the Public Health Department. The intensities at different times of the day and at different seasons are compared with European observations.

The main factors influencing the total amount of radiation received on a surface is the inclination of the surface and the altitude of the sun, the length of day and degree of cloudiness. Radiation intensity is increased by altitude above sea level. In summer, solar radiation is about the same in South Africa as in Europe but is much less in Europe than in South Africa during winter. A calculation is given showing that a ten-minute sunbath in South Africa is accompanied by the absorption of 60–70 Calories.

The chief effect of infra-red radiation is immediate heat erythema accompanied by blistering if there is over-exposure to the far infra-red rays. Metabolic changes affecting the blood sugar, sodium and phosphate levels have also been reported. It is concluded that the large amount of solar radiation reaching the earth's surface in South Africa must have physiological and psychological effects on its population.

The intensity of ultra-violet radiation is determined by the ozone content of the atmosphere, the turbidity of the air, and the thickness of the atmospheric haze. Sky radiation contributes as much as direct solar radiation. The total amount of ultra-violet radiation is 5–10 times greater in South Africa than in Europe. There is also a greater proportion of shorter wavelength radiation. The intensity of the lower ultra-violet wavelengths is much smaller when the sun is nearer the horizon. The wavelengths between 295 mμ and 320 mμ are biologically most effective.

Ultra-violet radiation produces several specific effects due to its actinic action. This action is mainly restricted to wavelengths shorter than 330 mμ. The "relative effectiveness" of a particular wavelength is a function of the biological effectiveness relative to the intensity of radiation at that wavelength. Curves are given showing the relative effectiveness for three different biological effects, *viz.* erythema, bactericidal action and ergosterol transformation. There is a notable increase in effectiveness with higher sun altitude.

The erythema effect would appear to aggravate the skin lesions in chicken-pox. This may be important in regard to other infectious diseases in the tropics.

If ergosterol behaves in the human skin as it does *in vitro*, a certain anti-rachitic effect can be expected even if the sun only rises to 15° as in Northern Europe in winter. South Africa obtains considerably more of this ergosterol transforming ultra-violet radiation, but whether there is too much of it in South Africa's sunshine will not be known until some idea has been formed as to the amount of natural radiation essential to produce an adequate vitamin D supply for adults. *A. F. Munro.*

WEINER, J. S. **The Regional Distribution of Sweating.** *J. Physiology.* 1945, June 29, v. 104, No. 1, 32–40.

This paper describes an attempt to partition sweat loss in three male subjects according to anatomical region. The men were in process of acclimatization to an effective temperature of 94°F. Profuse sweating was induced by continuous step-climbing during the first two hours of exposure, the effort being sufficient to raise the rectal temperature to slightly over 102°F. Observations were made during 50–60 minutes following the last work period, when rectal temperature was maximal.

Sweat was collected from a number of small areas on the head, trunk, thighs, legs, feet, arms and hands. Collection was made from three successive groups of ten areas, each group including areas from every region in order to reflect at each stage the rate of sweating from the body as a whole. The technique involved initial drying of the skin in the area selected, followed immediately by application of a metal ring 7 cm. in diameter and 2 cm. in depth. A well fitting lid prevented loss of sweat. The sweat samples were collected over periods of 2½ minutes, during the last 30 seconds of which they were mopped up on previously weighed cotton pledgets.

The difference between the observed overall sweat loss and the combined sweat loss calculated from the regional losses did not exceed ±8 per cent.

The general conclusions drawn from the experiments are as follows :—

(1) There are marked variations in the rates of sweating in different areas of each anatomical region, but approximately 50 per cent. of the sweat is lost from the trunk, 25 per cent. from the lower limbs, and 25 per cent. from the head and upper limbs.

(2) The rate of sweating is greater about the 8th day of acclimatization to heat than on the 3rd day.

(3) The " relative intensity " of sweating is calculated by dividing the proportion of total sweating contributed by a region by the proportion of total surface represented by that region. The " relative intensity " is greatest on the trunk, and next greatest on the head and varies on other areas according to the individual. Sweating is least on the hands, which are affected more by mental than thermal stimuli.

The author discusses how far these differences may be related to number, size or activity of the sweat glands. In the absence of experimental evidence, he suggests that in some areas, *e.g.* the trunk, there may be a greater reserve of " unused " glands or that individual glands may be on the average larger. [The author might have made the meaning of the term " relative intensity " clearer by stating that it is calculated by dividing the rate of sweating per unit area of a particular region by the mean overall sweating rate per unit area of the body.] *A. F. Munro.*

LADELL, W. S. S. **The Effect of Desoxycorticosterone Acetate on the Chloride Content of the Sweat.** *J. Physiology.* 1945, June 29, v. 104, No. 1, Proc. Physiol. Soc. 13P–14P.

" Daily intramuscular injections of 10–15 mg. of desoxycorticosterone acetate (DOCA) in man increase body weight and plasma volume, and reduce sodium and chloride excretion without changing serum sodium and chloride." " Diminished urinary sodium and chloride may be the result of a direct action on the kidney tubules." The author here shows that DOCA has an action on the sweat glands, and by collecting sweat and estimating its chloride, in subjects working in a hot room before and during a course of injections of DOCA (10 mgm. doses), found that about 30 per cent. less salt was lost in the sweat during the course than before it. The subjects of the experiment gained weight and became oedematous, but the effect passed off 72 hours after the last injection. *Charles Wilcocks.*

TROPICAL ULCER.

VINCENT, Hyacinthe. Remarques sur l'étiologie, la pathogénie et l'agent pathogène, " Bacillus fusiformis," de l'ulcère phagédénique. [**The Aetiology, Pathogeny and Pathogenic Agent,** *Bacillus fusiformis*, **of Phagedaenic Ulcer.**] *Bull. Acad. Méd.* 1945, v. 129, Nos. 30, 31 & 32, 545–8.

The author was surprised to read in a recent paper by BALOSET, DURAND and RAGU (*Bull. Acad. Méd.*, 1945, v. 129, 533) that there are two types of *Bacillus fusiformis*, the non-motile type of Vincent and the motile type of Plaut. Both motile and non-motile forms were described by Vincent, who found them together in the same microscopic field ; as for Plaut's bacillus, the latter observed " Miller's bacilli," which were really *Spirillum sputigenum*, previously described by several authors, and quite different from *B. fusiformis* and from *Spirochaeta vincenti*.

Phagedaenic ulcer according to the author is caused by *B. fusiformis* frequently in association with *Sp. vincenti* and other micro-organisms, especially staphylococci, and streptococci. When material from an ulcer was injected into the healthy tissues of healthy guineapigs and rabbits, no ulcer was produced, but when the injection was made into the previously crushed tissues of these animals which had been kept on a low diet for a few days, and especially when other organisms—staphylococci, streptococci or *Pseudomonas pyocyanea*—were also injected at the same time, typical ulcers were produced.

In the tropics ulcers occur in persons who are debilitated by such causes as malnutrition, excessive fatigue, or some other infection ; some races are more susceptible to the infection than others.

The author has successfully treated phagedaenic ulcer by first cleaning it with normal saline, then drying it and applying a mixture of dry powdered calcium hypochlorite, 1 part, and dry boric acid powder, 9 parts ; the dressing was renewed every 3 or 4 days. The surrounding skin was painted with tincture of iodine. A suitable diet was prescribed. Healing usually took place in 2 or 3 weeks. *J. F. Corson.*

MOHANTY, J. K. **So-called Tropical Ulcer in Angul.** *J. Indian Med. Ass.* 1945, Aug., v. 14, No. 11, 263–6 & 262, 1 graph & 1 fig. [17 refs.]

The occurrence of tropical ulcer in Angul, India, had not been reported before 1942, but in that year and the following one many cases occurred ; the

infection appeared to have been introduced from Assam by returning soldiers [see also this *Bulletin*, 1944, v. 41, 614 ; *ibid.*, 1945, v. 42, 405]. Poverty-stricken, badly nourished people, nearly all men, were chiefly affected.

Smears taken from the ulcers showed abundant diphtheroid bacilli ; in 4 cases *Bacillus fusiformis* was present without diphtheroids. No facilities for culture were available but " several experiments were done on the patients and on pigeons." Ulcer discharge fluid containing diphtheroids was injected intradermally and produced typical ulceration in 7–8 days, and the same result was obtained by injecting conjunctival discharge containing diphtheroids ; if the material injected was previously heated, no ulcers were produced. The injection of diphtheroid-containing material into the chest muscles of pigeons caused inflammation and fever and the birds died in 2-5 days.

No immunity apparently developed ; other ulcers occurred, even during convalescence.

The leg and the dorsum of the foot were chiefly affected ; in a few cases the ulcer was on the elbow, forearm or thigh, but none was seen on the sole or on the face. Regional lymphatic glands were not involved. No peripheral neuritis was observed.

Treatment.—Many applications were tried but none seemed better than another ; a simple daily dressing with complete rest of the limb was beneficial. The injection of 4,000 units of antidiphtheritic serum daily for 3 days had no apparent effect on the ulcers. *J. F. Corson.*

Seshadrinathan, N. **Tropical Ulcer. A Study of One Hundred Cases collected in the City of Madras.** *Indian Med. Gaz.* 1945, July, v. 80, No. 7, 344–6.

The author made observations on 100 cases of tropical ulcer in the city of Madras. The size of the ulcers varied from $\frac{1}{4}$ in. to $2\frac{1}{2}$ ins. in diameter, 73 out of 84 not exceeding 1 in. ; of 95 ulcers, 62 were on the foot, 32 on the leg and 1 on the elbow. The ulcers were painful and very tender. The ages of the patients ranged from 7 years to over 50 years. Thirty were weavers by trade and only 4 of these gave a history of trauma as a cause of the ulcer, whereas half of the others gave such a history. The weavers work with their legs in long pits in which the handlooms are lodged ; the pits are warm and moist and lined with cow-dung, but it is not known whether insects took shelter in the pits. Persons of the class of the patients drink little or no milk.

Spirochaetes and fusiform bacilli were present in the ulcers, the longer forms of the fusiform bacilli being motile ; pure cultures of fusiform bacilli were grown on 1 per cent. agar containing 25 per cent. of rabbit blood, incubated at 37°C. in an atmosphere of 90 per cent. of hydrogen and 10 per cent. of carbon dioxide, but subcultures could not be maintained.

In treatment the best results were obtained with gauze soaked in a warm 5 per cent. solution of copper sulphate. *J. F. Corson.*

MISCELLANEOUS DISEASES.

Ogilvie, W. H. **Pitfalls of Tropical Surgery.** *Lancet.* 1945, Nov. 10, 585–7.

The author was a consulting surgeon to the East Africa Force in 1940–42 and to the Middle East Force in 1942–44 and discusses some of the puzzling aspects of surgery which he encountered in Africa ; he selects as subjects three diseases—amoebiasis, malaria, and bilharziasis—and the peculiarities of the African as a patient.

Amoebiasis is generally seen by the surgeon in a chronic stage; in two patients an amoebic abscess of the liver simulated gall-stones, and two cases of intussusception, beginning at an amoebic mass in the caecum, were seen, while an amoebic mass in the rectum was mistaken for a carcinoma and a left inguinal colostomy was performed. The author suggests that toxic absorption from the ulcerated bowel may cause subacute arthritis of the synovial type. Operation for haemorrhoids, fistula or anal fissure should not be done within two months after the end of an attack of dysentery, and not without preliminary sigmoidoscopy.

Malaria complicates surgical diagnosis and disturbs treatment; post-operative and post-traumatic rises of temperature are almost universal in malarial countries. In abdominal conditions particularly diagnosis is made more difficult.

Bilharziasis was probably responsible for failure to catheterize the ureters on many occasions; several instances of bilateral dilation of the ureters were seen in South African officers.

The African "appears to be a biological species distinct from Northern man"; the author notes his freedom from arterial disease, duodenal ulcer and parasyphilis even when he adopts town life. The African suffers from acute arthritis and bone disease which appear to be due either to syphilis or yaws. Primary carcinoma of the liver is common among the Bantu races. The author concludes with the sentence "But the standard textbook on tropical surgery has yet to be written." *J. F. Corson.*

WILLSON-PEPPER, J. K. **Impressions of Surgery in West Africa.** *Brit. Med. J.* 1945, Dec. 8, 812–14.

The author was a surgeon at a hospital in a swampy, mosquito-infested region of West Africa for 19 months; his patients were nearly all European troops and he found unexpected differences in the course of surgical diseases and the effect of treatment from what he had previously experienced in temperate climates, staphylococcal infections, for example, being particularly severe. In this paper he records his general impressions received during that period of work in tropical Africa. *J. F. Corson.*

CROPPER, C. F. J. **Amoebiasis.** [Correspondence.] *Brit. Med. J.* 1946, Feb. 2, 181.

The author disagrees with the opinion of WILLSON-PEPPER [above] that the proctoscope may be used instead of the sigmoidoscope, with equal results, for the diagnosis of amoebic dysentery; in his experience the only visible lesions "in a very large percentage of cases" are at 5 to 6½ in. from the anal margin. He agrees that exhausting wash-outs should not be given before the rectal examination but considers that two or three *weak* soap or bicarbonate enemas may be given three hours before the examination [with the sigmoidoscope] with advantage. *J. F. Corson.*

VISWANATHAN, R. **Pulmonary Eosinophilosis.** *Indian Med. Gaz.* 1945, Aug., v. 80, No. 8, 392–6. [11 refs.]

The condition here dealt with has several synonyms: pseudo-tuberculosis with eosinophilia, benign eosinophilic leukaemia, tropical eosinophilia, eosinophil lung, and the author now suggests another, a variant of the last, namely, pulmonary eosinophilosis. He gives a brief review of 85 cases seen during a period of 14 months among nearly 1,000 admissions to hospital for respiratory

troubles. Though they originally came from different Provinces, all had been in East Bengal or Assam recently for 3 months or more, so a humid climate may play some part in the aetiology. The chief symptom was troublesome but unproductive cough, with fever in 51 (60 per cent.) and sometimes asthma-like attacks. Physical signs were few ; basal râles and slight tachycardia, and rhonchi in the " asthmatic ". Eosinophiles constituted 15 to 80 per cent. of a total leucocyte count of 10,000 to 50,000. X-rays showed small disseminated shadows, but these are seen in the acute phase only and their absence does not exclude the diagnosis. The blood often gave positive " cold agglutination " of pneumococci, as in some cases of atypical pneumonia. Occasionally there were unusual features such as widespread lymphadenitis, pleurisy with effusion, palpitation and praecordial pain. Arsenicals bring about a speedy cure, though the first injections increase the eosinophilia. The usual method is an initial dose of 0·15 gm. NAB and twice this every 5 days after till symptoms disappear.

As regards causation the author considers previous suggestions of mites (as found by CARTER, WEDD and D'ABRERA, see this *Bulletin*, 1945, v. 42, 73) ; he looked for them without success in 6 of his cases ; atypical pneumonia (because of the high titre cold agglutination test) and the inevitable virus.

H. Harold Scott.

FARIS, R. A. **Eosinophilic Infiltration of the Lung (Report on Two Cases).** *J. Palestine Arab Med. Ass.* 1945, Nov., v. 1, No. 1, 17–20.

BENT, M. J., TURNER, E. L., HOLLOWAY, G. D. & CUFF, J. R. **Nutritional Deficiency as an Etiological Factor in Icterus accompanying Pneumonia in the Negro. II. Value of Brewer's Yeast in preventing Icterus in Pneumonia.** *Southern Med. J.* 1945, Nov., v. 38, No. 11, 730–33. [12 refs.]

From clinical evidence and experiments on dogs the authors [this *Bulletin*, 1944, v. 41, 148] concluded that a high incidence of jaundice in a group of adult negroes was due to a badly balanced diet associated with poor cooking. In the present paper experiments to test the protective action of the vitamin B complex when added to the same deficient diet as was used in the previous experiments, are recorded.

Nine dogs (controls) were placed on the restricted diet only, and 11 other dogs were given the same diet with the addition of brewer's yeast. After the dogs had been on the diets for 21–49 days, pneumonia was induced by the insufflation of pneumococci (Type 1, Robertson strain). Van den Bergh tests were made daily before the insufflation and twice daily afterwards. The dogs were killed and examined one to four days after the insufflation.

None of the 11 dogs on the diet plus yeast developed a positive van den Bergh reaction, while all the 9 controls did. All the control dogs lost weight while none of the others did, and 5 of them gained weight ; the former, however, rejected more and more of their food as time went on.

Post-mortem examination showed that all the 9 controls had pneumonia and extensive fatty changes in the liver ; the other 11 dogs had less severe pneumonia, 5 of them showed no pathological changes in the liver and only one showed changes comparable with those observed in the controls.

The results support the conclusions reached in the previous observations and experiments.

J. F. Corson.

DESPUJOLS, B., BERGERET, C., CALMET, L. & ROUVIER, J. Sur un cas de mélioidose à évolution prolongée. [**A Case of Melioidosis with Prolonged Course.**] *Méd. Trop.* Marseilles. 1942, Nov., v. 2, No. 9, 689–702. [10 refs.]

GENERAL PROTOZOOLOGY.

KIRBY, H. **The Structure of the Common Intestinal Trichomonad of Man.** *J. Parasitology.* 1945, June, v. 31, No. 3, 163–75, 27 figs. on 3 pls. [18 refs.]

The author has studied cultures of two strains of trichomonas of the human intestine, employing dark-field illumination and films fixed in Hollande's cupric picroformal and impregnated with silver by activated protargol, as recommended by BODIAN for nervous tissues and adapted to protozoological technique by COLE and DAY. By the impregnation technique a flattened structure not hitherto described was found at the anterior end of the body. It is termed the pelta. It lies to the right of the blepharoplast-complex and is continued as a filament in the cytoplasm dorsal to the nucleus. A small ellipsoidal parabasal body lying against the anterolateral surface of the nucleus was also demonstrated. In other respects the findings are mainly in agreement with those of WENRICH [this *Bulletin*, 1944, v. 41, 697, 698], particularly with regard to the existence of five anterior flagella, four of which, directed forwards, have a common origin in the blepharoplast-complex, while the fifth originates independently from this complex and is directed laterally or posteriorly. The author follows WENRICH " in his opinion that there is one species that is commonly found in the intestine of man ; and, in fact, there are grounds for surmising that there is a possibility that all accounts of trichomonads from that situation, except that of *Tritrichomonas faecalis*, have actually dealt with the one species." The author considers that the presence of 5 flagella, one of which arises independently of the others, justifies the use of the generic name *Pentatrichomonas*, the intestinal trichomonad of man being denominated *Pentatrichomonas hominis* (Davaine, 1860). The paper is illustrated by a series of drawings and microphotographs showing the various structures revealed by the technique employed. *C. M. Wenyon.*

TRUSSELL, R. E. & JOHNSON, G. *Trichomonas vaginalis* **Donné. Recent Experimental Advances.** *Puerto Rico J. Pub. Health & Trop. Med.* 1945, Mar., v. 20, No. 3, 289–305, 6 figs. on 2 pls. [Refs. in footnotes.] [Spanish version 306–21.]

CALLAHAN, W. P., Jr. **The Incidence of Toxoplasmic Infections in the St. Louis Area.** *Proc. Soc. Exper. Biol. & Med.* 1945, May, v. 59, No. 1, 68–70.

As cases of toxoplasmosis seemed to be of fairly frequent occurrence in the St. Louis area of U.S.A. the author decided to test sera from apparently healthy individuals by Sabin's neutralization method, in which varying dilutions of serum mixed with toxoplasms are inoculated into the skin of rabbits. Eight fatal cases of toxoplasmosis had been observed in St. Louis since 1940. Two were in adults who suffered from an acute febrile condition associated with a skin rash, resembling the typhus-spotted-fever group of diseases. The other cases were in infants in whom the disease was apparent at birth or commenced soon after. There was widespread involvement of the central nervous system giving rise to generalized convulsions, muscular paralysis and internal hydrocephalus. Cerebral calcification and encephalomyelitis with the formation of many granulomatous lesions were the chief pathological changes. Toxoplasms were present in small aggregates or in pseudocysts and as free organisms in the central nervous system. Of 100 sera tested, 74 were from inhabitants of St. Louis and 26 from persons outside the state of Missouri. Only two of these sera prevented the production of skin necrosis by the toxoplasma injected.

These were from unmarried girls, 18 and 21 years of age, of the St. Louis area. Neither showed any evidence of present or past illness which might be interpreted as toxoplasmosis. *C. M. Wenyon.*

Weinman, D. La toxoplasmosis en el hombre. [**Toxoplasmosis in Man.**] *Día Médico.* 1945, Oct. 8, v. 17, No. 41, 1164–70, 2 figs.

GENERAL ENTOMOLOGY.

Haddow, A. J. **The Mosquitoes of Bwamba County, Uganda. III. The Vertical Distribution of Mosquitoes in a Banana Plantation and the Biting Cycle of** *Aëdes* **(*Stegomyia*) *simpsoni*, Theo.** *Bull. Entom. Res.* 1945, Nov., v. 36, Pt. 3, 297–304, 3 figs.

The vegetation and climate of the Bwamba area were described in Part I, and the activity of the local mosquitoes was dealt with in Part II, of this series of papers [see this *Bulletin*, 1946, v. 43, 79, 80]. The third part is mainly concerned with the biting activities of *Aëdes simpsoni* (the vector of human yellow fever in Bwamba) at different vertical levels.

Four catching stations were established near a large banana plantation. One was on the ground among heavy undergrowth, the other three were on platforms in the trees. The first of these was erected at six feet from the ground among leaves of young plants, the next was at 12 feet among leaves of full-grown plants, and the highest was at 18 feet in the open air above the tallest plants.

The catching of mosquitoes from human baits at all four stations was done simultaneously and continuously for ten days, five of which were hot and bright with cold mornings, and the other five warm and cloudy with warm mornings. Catches for each hour from each level were recorded separately.

The total catch was 687 mosquitoes, belonging to 16 species (counting the mixed *Culex* spp. as one). The vertical distribution of all species was as follows: 210 (eleven species) at ground level; 182 (nine species) at 6 ft.; 167 (seven species) at 12 ft., and 128 (six species) at 18 ft. *Aëdes simpsoni* accounted for 596 of these as follows: 179, 159, 141 and 117 at the respective levels. Other species were so scarce that their numbers were inadequate for discussion, but it is noted that sylvan species such as *Anopheles implexus* (1) *Aëdes apicoargenteus* (1) and *Aëdes africanus* (3) were present in the catches though the nearest breeding places of *Aëdes apicoargenteus* and *Aëdes africanus* were in the forest half a mile away, where larvae were abundant in tree-holes.

By grouping the catches in hourly and four-hourly periods, it is shown that *Aëdes simpsoni* is a strictly diurnal species, most active on the warm cloudy days, which produced 445, as against 151 for the hot bright days with cold mornings.

The principal raiding monkey in Bwamba is *Cercopithecus nictitans mpangae* Matschie, the common red-tail or white-nosed guenon. Out of 41 of these monkeys, 25 were found to be immune to yellow fever, and it is suggested that an infected monkey feeding on the bananas at the 12-ft. level could easily pass on the yellow fever virus to *Aëdes simpsoni*. *H. S. Leeson.*

Adam, N. K. **A Rapid Field Method for assessing the Spreading Power of Anti-Malarial Oils.** *Bull. Entom. Res.* 1945, Nov., v. 36, Pt. 3, 269–72.

It is essential that an oil used for killing mosquito larvae should spread completely over the surface of the water to be treated. Most natural waters,

especially if stagnant, are already covered with a film, either visible or invisible, which the spreading oil must push aside. The efficiency of the antimosquito oil, therefore, depends to a large extent on its spreading pressure. In the laboratory this can be measured directly in dynes per centimetre (see ADAM, *Proc. Roy. Soc.* B, 1937, v. 122, 134) but it is often important to use a more simple method, and portable apparatus, especially in the field.

The method suggested employs a prepared series of liquids of standard spreading pressure. These are either compared with an unknown liquid on a clean surface, or tested against a natural film ; the substance producing a film with the greater pressure will push back the other film. In the laboratory, rapid tests are made with a large glass funnel, cleaned and kept clean by water overflowing round the rim from a supply through the stem. The water flow is stopped and a little water tipped out to lower the level just below the rim ; a drop of one oil is applied to the surface, covering it with a film and leaving a lens of about a quarter of an inch in diameter. The second liquid is then added and the effect observed : if necessary talc powder can be shaken on to facilitate observation of movements of the films.

The liquids of choice for the standards may be used alone or as solutions in non-spreading mineral oil (medicinal paraffin). They must not be volatile and they must not be affected by the *p*H range to be expected in natural waters. The following series are recommended :—

Standard Spreading Liquids.

	Spreading pressure, dynes per cm., 20°C.
Methyl *or* ethyl salicylate	13
Dimethyl *or* dibutyl phthalate	21
Terpineol, liquid (from B.D.H. Ltd.)	36
Oleyl alcohol (from I.C.I. Dyestuffs Ltd.)	47

Standard Spreading Solutions.

Solvent : B.D.H. Liquid paraffin S.G. 0·835–0·850.

Terpineol in paraffin		Oleyl Alcohol in paraffin	
cc. Terpineol per 100 cc. sol.	Sp. pressure dynes/cm. 20°C.	gm. Oleyl Alcohol per 100 cc. sol.	Sp. pressure dynes/cm. 20°C.
0·1	4·5	0·2	12
0·2	7·5	0·5	17
0·5	13	1·0	25
1·0	18	2·0	30
2·0	21	5·0	37
5·0	25	10·0	46
10·0	30		

J. R. Busvine.

HOEHN, D. **Nephrosis probably due to Excessive Use of Sta-way Insect Repellent.** *J. Amer. Med. Ass.* 1945, June 16, v. 128, No. 7, 513.

A white boy, aged 3 years, was admitted to hospital on 4th August, 1944, acutely ill with generalized oedema. His urine contained pus and albumin but no casts. He improved for a few days, then the oedema increased and by September he appeared to be dying. He was given four plasma infusions and two blood transfusions, after which he gradually improved and at the time of writing was in fairly good health.

During the whole of the summer an insect repellent called " Sta-way " had been freely applied to his skin ; tests were made on rabbits and it was found that " Sta-way " was a strong kidney and liver poison.

The author concluded that the child had suffered from nephrosis due to the application of " Sta-way ". *J. F. Corson.*

Niño, F. L. & Fernandez, J. C. Miasis cutánea por larvas de " Cochliomyia hominivorax " (Coquerel, 1858). [**Cutaneous Myiasis due to** *C. hominivorax*.] *Bol. Inst. Clín. Quirúrg.* Buenos Aires. 1945, May, v. 21, No. 173, 281–6, 8 figs.

Stanbury, J. B. & Huyck, J. H. **Tick Paralysis : a Critical Review.** *Medicine*, 1945, Sept., v. 24, No. 3, 219–42. [77 refs.]

LABORATORY PROCEDURES.

Mertens, Elizabeth. **A Simple Technique of Sternal Marrow Biopsy for Spreads and Sections.** *Amer. J. Med. Sci.* 1945, Nov., v. 210, No. 5, 630–34, 6 figs.

The author describes a method of sternal marrow aspiration which has most of the advantages of both the aspiration and the trephine methods, without their disadvantages ; it resembles the aspiration method but differs in that the blood is allowed to clot and sections can therefore be made.

The skin, subcutaneous tissues and periosteum having been anaesthetized with 1 per cent. novocain solution, a 15 gauge Osgood sternal puncture needle is entered in the mid-sternal line at the level of the upper border of the 3rd costal cartilage. The stylet is removed when the marrow cavity is reached and the needle is then gently pushed on at an angle of 30 to 40 degrees for not more than 7 mm. in an adult, or until the resistance of the posterior lamella is felt. A dry 10 cc. syringe is then attached and sternal marrow and blood are aspirated to a height of 2–3 mm. in the syringe. The tip of the syringe should have a bore equal to that of the needle. The syringe is detached and the plunger withdrawn for about 1 cm. and the contents allowed to clot ; when clotting is complete the plunger is withdrawn with the attached clot, which is then put into fresh Zenker's formol solution for fixation. Paraffin sections are cut and stained with Azure II Eosin.

To obtain films the needle is withdrawn as far as the anterior lamella, the stylet removed, and the needle passed again into the marrow cavity in a slightly different direction ; a second syringe is attached, a second specimen aspirated, the stylet reinserted, and the needle removed. *J. F. Corson.*

REPORTS, SURVEYS AND MISCELLANEOUS PAPERS.

Sicé, A. Role social du médecin colonial en Afrique Française. [**The Social Function of Colonial Medical Officers in French Africa.**] *Méd. Trop.* Marseilles. 1944, May–June–July–Aug., v. 4, No. 3, 185–93.

The French language is perhaps the most perfect medium for dignified and persuasive prose, and General Sicé is a master of its use. His theme is worthy

of the language he uses, and in this short paper he makes several points which should more and more command the attention of colonial medical men and administrators alike ; they carry the more weight because they are the result of many years of active work in various countries of the French Colonial Empire. The first point is that the activities hitherto undertaken to develop the colonies have been concerned too much with political and economic matters, and too little with care for the people as human beings. Workmen have been engaged for labour in strange districts, where the tendency has been for them to lose contact with their own tribes and to succumb to the single object of earning only enough to maintain life at its lowest, having lost touch with those family and tribal activities which afforded interest in their own homes, and having no substituted interest to which they could satisfactorily turn. The attitude has been short-sighted in that little note has been taken of the fact that the man who is interested in his work for its own sake is the best workman. In such cases failure to make provision for the *moral* of the workman has led to his decadence. It is the function of the medical man to study and take care of the mind no less than of the body, and medical men can see more clearly, perhaps, than any others the disabilities which come to individuals and to the community, as a result of a feeling of neglect or exploitation. Sicé insists on the fact, too often overlooked, that the Africans have feelings, desires and ambitions like those of white men, and that these factors of their humanity can be disregarded only at the peril of decadence. A country populated by people who have lost interest would not be an asset ; the quality of work depends as much on mental as on physical condition.

Sicé brings out the most important point that medical men should be given a much greater share than at present they possess in the formation of policies ; that the direction of affairs in the colonies should be determined more by their effect on mental and physical health than is now the rule. He quotes a case in point. In the French Cameroons one area was severely affected by trypanosomiasis, and the authorities took the unusual step of entrusting the whole administration to the colonial medical service, with most remarkable results. Sleeping sickness was almost eradicated, and the comprehensive measures taken to improve health in every direction transformed the people, in the short space of four years, into a healthy and vigorous community, with the result that prosperity returned.

Finally, Sicé quotes Terence :—*Homo sum ; humani nil a me alienum puto.* Colonization is a human activity, one of whose primary aims is to assure to the indigenous inhabitants health, vigour and prosperity, and every activity of the people and the government has a bearing on health, and is therefore the concern of the doctor.

[General Sicé has achieved scientific distinction during his long period of colonial service, but can have made no greater contribution to medical thought than is outlined in this short paper. His views are in accord with those of the West India Royal Commission (this *Bulletin*, 1946, v. 43, 70) ; they should be studied by administrators and medical men alike.] *Charles Wilcocks.*

Sautet, J. & Marneffe, H. Notes sur le paludisme, la bilharziose intestinale, les teignes, etc., au Soudan Français. (Documents recueillis en Septembre-Octobre 1942 au cours d'une mission du Secrétariat d'Etat aux Colonies suivis de quelques résultats d'ensemble de la mission.) [**Notes on Malaria, Intestinal Schistosomiasis, Ringworm, etc., in the French Sudan.**] *Méd. Trop.* Marseilles. 1943, Sept.-Oct., v. 3, No. 5, 343–67, 23 figs. on 8 pls., 2 text figs. & 1 map. [23 refs.]

KLEINE, F. K. Ärztliche Forschungsreisen in Afrika. [**Medical Research Journeys in Africa.**] *Deut. Tropenmed. Ztschr.* 1944, June, v. 48, Nos. 11/12, 244–61.

The author visited Northern Rhodesia and the Belgian Congo in 1921–3 for the purpose of testing the action of the recently discovered compound " Bayer 205 " on trypanosomiasis in naturally infected human beings and domestic animals. The published results of the work of this expedition were abstracted in this *Bulletin*, 1923, v. 20, 317 & 322 ; 1924, v. 21, 56 (also 380 & 763).

The present account is mainly a story of the journey ; in it the author describes the various incidents and difficulties of travel in tropical Africa which he and his companions experienced—on foot, by lake steamer, and by train. He makes observations on the different territories visited, their natural features, fauna and inhabitants and mentions European officials and others whom he met and who helped him in many ways.

His work was completed by September 1923, and at the end of his travels there remained, as he expresses it, " die neu genährte Sehnsucht nach Afrika, nach seiner strahlenden Sonne und seiner grossen Freiheit " [a longing which the abstracter has often heard him express]. *J. F. Corson.*

FISCHER, L. Arztliche Erfahrungen in Afghanistan, zugleich ein Beitrag zur Krankheitsgeographie Mittelasiens. [**Medical Experiences in Afghanistan : a Contribution to the Geography of Disease in Middle Asia.**] *Deut. Tropenmed. Ztschr.* 1944, June, v. 48, Nos. 11/12, 209–44. [133 refs.]

The author, Professor L. Fischer of Tübingen, Germany, a senior naval medical staff officer, was engaged in medical work in Afghanistan, chiefly in Kabul, from 1938 to 1941, when he was compelled by the war to return, and left his records behind in Kabul. The present paper on medical progress and disease in Afghanistan contains, therefore, few statistics. In a previous paper [this *Bulletin*, 1944, v. 41, 313] he gave a short account of native medicine in that country.

In recent years the Afghan government has encouraged the introduction and development of Western European civilization ; there are English, French and German high schools in the country, and Afghan pupils have gone to study in European high schools. Medical education has similarly progressed. Indian and Turkish doctors were followed by Germans ; in 1939 there were three German doctors, two men and a woman, practising in the country. Afghan students studied medicine in Europe. To meet pressing needs a medical school was founded ; it gave a three-years' course of study, enabling students to become assistants though they were not regarded as fully qualified doctors. Later, a small medical faculty under Turkish direction was formed in Kabul ; here a five-years' course was given for full medical qualification. During the author's residence there were about 50 medical students.

The Minister of Health, with medical advisers, controls the medical services of the country. Hospitals were built in the towns ; in Kabul they included separate hospitals for men and women, a sanatorium for chest diseases, a Roentgen institute, a dental hospital, and a hygiene and bacteriological institute. In the smaller towns the hospitals, numbering about 20, were of simpler type but had accommodation for in-patients. Numerous polyclinics were also built. To serve the villages it was proposed to appoint a travelling doctor, but the plan was prevented by the war.

In Kabul a town health service was established under German direction. The town authority took over from the Minister of Health three polyclinics

situated on the outskirts of the town; in the years 1938–1941 the average monthly numbers of patients treated were 950, 1,950, 3,020 and 3,700, and in the summer of 1941, over 5,000.

Kabul, an old town with a population of 140,000, has many narrow, crooked, unpaved streets and houses built of mud; it has, however, a pipe-borne water supply brought from the mountains about 20 miles away. The water is good and is periodically examined, and, if an epidemic is threatened, it is chlorinated. The water supply is insufficient for modern needs and the new houses in the suburbs have water tanks which are filled daily. The drainage of surface and waste water is primitive but in the newer parts covered soakage pits in the dry porous soil are satisfactory. The latrines are simple pits.

Some years ago the lay-out of a new town was begun; it was originally planned as a university town with modern construction, sanitation and water supply.

The duties of the health officer include street cleaning, supervision of markets, slaughter houses, and food bazaars, bath houses and the drainage of waste water; in addition there are preventive measures against malaria, cholera, smallpox and trachoma, and efforts to obtain greater care of infants and small children. As in some other Mohammedan countries the seclusion of women is a hindrance to medical progress.

Modern Afghanistan strives to keep in touch with Western European science; a "Review of Hygiene" in the Persian language has been published for some years. In the author's time some Afghan students who had studied in Europe, together with some French naturalists in Afghanistan, founded a society for the study of valuable products of the earth—minerals, medicinal plants, and medicinal springs; this had the interest and support of the Ministers of Health and Agriculture.

The author describes briefly the chief infectious and non-infectious diseases of the country. *Malaria*, benign tertian and subtertian, is widespread; quartan malaria is unknown and there is no record of *blackwater fever*. Little is known of anopheline vectors. *Kala azar* is not known to occur but cutaneous leishmaniasis is present and *Phlebotomus* abounds; it is unknown whether canine leishmaniasis exists in the country. *Trachoma* is very common; in Kabul it affects about 13 per cent. of the population. *Relapsing fever* of the Persian type, probably tick-borne, occurs in the spring and early summer. *Typhus*, never in epidemic form, is present from January to April, *typhoid* and *paratyphoid* A and B, in the late summer, autumn and first part of the winter. *Bacillary* and *amoebic dysentery* occur, the latter being widespread; though amoebic carriers were found among the Germans resident in Kabul, no amoebic dysentery is known there. *Shiga-Kruse*, *Flexner*, and *Sonne* types of dysentery bacilli, *Salmonella breslau* and *Bact. faecalis alkaligenes* have been isolated. Acute intestinal diseases cause a large part of the high mortality among small children. *Cholera*, *smallpox* and *plague* occur sporadically; in 1938, an outbreak of cholera occurred, with 3,291 cases and 1,710 deaths; nearly half a million persons were vaccinated and there was no outbreak in the following year. *Undulant fever* and *abortus fever* are not known to occur. *Leprosy* is present but its extent is unknown; it is estimated that there are from 1,200 to 3,000 cases in the whole country. It was proposed to form a leper settlement, largely self-supporting, about 10 miles from Kabul, but the war prevented the carrying out of the plan. Little is known of the prevalence of *venereal disease*; the author saw only a few cases of syphilis and gonorrhoea in Kabul. Few cases of *diphtheria* and *scarlet fever* are seen, but *measles* is prevalent and ranks after *smallpox* and *whooping cough* as a fatal disease in children. *Tuberculosis* in Kabul appears to resemble the disease in Europe

in its incidence and course ; extrapulmonary tuberculosis appears to be rather common. Various other cosmopolitan diseases occur and call for no special mention.

The author thinks that the high mountain ranges on the eastern side form an epidemiological barrier as well as a geographical one ; in its epidemiology Afghanistan resembles the countries on the western side where there are few geographical barriers. The paper contains many references to medical reports of neighbouring countries. *J. F. Corson.*

Notestein, F. W. & Jurkat, E. **Population Problems of Palestine.** *Milbank Memorial Fund Quarterly.* 1945, Oct., v. 23, No. 4, 307–52, 18 figs.

BOOK REVIEWS.

Ackerknecht, E. H. **Malaria in the Upper Mississippi Valley 1760–1900.** *Suppl. to the Bull. History of Med.* 1945, No. 4, pp. viii + 142, with maps & figs. [Bibliography.]

The Upper Mississippi Valley is one of those interesting regions from which malaria, once very prevalent, disappeared long before the introduction of any systematic antimalarial measures and largely before the acquisition of knowledge of its mode of transmission. In this very interesting monograph the author has gathered together a surprisingly large amount of information from records of the early days of the conquest and settlement of the great continental heart of North America, when " ague " was so formidable a menace to health along the rivers which constituted the chief means of communication. From then up to recent times the records have been searched for information bearing on this fascinating epidemiological problem, and the search has been fruitful.

The five States included in this area, Illinois, Missouri, Iowa, Wisconsin and Minnesota, are each described and considered independently ; a map of each State is attached. Then the factors which may have contributed to the elimination of the scourge of malaria are discussed in turn and numerous authorities are quoted. The factors considered are : population movements ; steamships, railroads and river regulation ; clearing, cultivation and drainage ; prosperity ; housing ; screening ; food ; education ; cattle breeding ; mosquitoes ; quinine ; climate. Clear and concise answers to the innumerable questions raised in inquiries of this nature are hardly to be expected, but the author does show that the arrest of population movements was accompanied by a decline of malaria incidence in Missouri, Iowa and Wisconsin. Another important factor was the shifting of settlements away from watercourses that resulted from the construction of railroads. Drainage enterprises may have speeded up the decline of malaria in Illinois, but elsewhere the decline preceded organized drainage. Better housing and an increase in dairy cattle characterized the period of malaria decline. To quote the author's concluding words " it may be well to remember that malaria in the Upper Mississippi Valley was not killed by a single magic bullet ; the monster was only put in chains, the links of which we have tried to study. Each link of the chain is important and the breaking of one link may set free again the evil fiend." But, as the author repeatedly states, the climate in the Valley is not very favourable for malaria. *Norman White.*

CASTILLO, Roberto Leví. **Los anofelinos de la Republica del Ecuador.** Vol. 1. 172 pp., numerous figs., maps & pls. 1945. Guayaquil-Ecuador : Artes Graficas Senefelder C. A. Ltda.

This is a systematic and adequate description of the *Anopheles* hitherto recorded in the Republic of Ecuador. An introduction details the salient geographical features of the country and the climatic conditions. The equator traverses the north of Ecuador. The three natural geographical regions of the country are : a coastal region between the Pacific Ocean and the western escarpment of the Andes, comprising the provinces of Esmeraldas, Manabi, Guayas, Los Rios and El Oro ; a mountainous, Andes, region comprising the provinces of Carchi, Imbabura, Pichincha, Cotopaxi, Tungurahua, Chimborazo, Bolivar, Cañar, Azuay and Loja ; and an eastern Amazon region wedged in between Colombia and Peru and the eastern escarpment of the Andes, and comprising the provinces of Napo-Pastaza and Santiago-Zamora. The species of *Anopheles* found in these three regions are : Western coastal region, *A.* (*Chagasia*) *bathanus*, *A. pseudopunctipennis levicastilloi*, *A. eiseni*, *A. punctimacula*, *A. apicimacula*, *A. mediopunctatus*, *A. albimanus*, *A. aquasalis* and *A. neivai* : Central Andes region, *A. pseudopunctipennis rivadeneirai*, and *A. eiseni* : Eastern Amazon region, *A. boliviensis*.

All these species are fully described and illustrated. *A. albimanus* is the main vector of malaria throughout the coastal provinces, where it is very widespread ; infection rates of from 3 to 5 per cent. have been recorded. The author believes that Ecuador is the southern limit of distribution of *A. bathanus* ; it has never been reported from Peru. Of the two races of *A. pseudopunctipennis* found in Ecuador *A. pseudopunctipennis rivadeneirai* is the chief vector of malaria in the warm highland valleys : it is found in all the provinces of the central Andes region and has been found as high as 2,500 metres. It has a marked preference for human blood. In contrast *A. pseudopunctipennis levicastilloi* exhibits marked zoophilism ; it is not found at altitudes above 300 metres. *A. eiseni* is a wild species and is zoophilic ; it has been found at altitudes ranging from 86 to 2,100 metres. *A. apicimacula* was found in five of the central Andes provinces ; it is zoophilic and is only met in jungle far from human habitations. *A. mediopunctatus* occurs in coastal jungles but is very rare. *A. aquasalis* is the only species found breeding in brackish water in Ecuador ; it breeds in crab holes in banks of inlets from the sea in the coastal provinces. *A.* (*Kerteszia*) *neivai* breeds exclusively in bromeliads in the five coastal provinces. *A.* (*Kerteszia*) *boliviensis*, of similar breeding habits, is very abundant in the Amazon provinces of Ecuador. It frequents human dwellings and has a preference for human blood ; it is a suspected vector of malaria.

The numerous photographs appended to this small volume are very indifferent and add nothing to its value. *Norman White.*

FINNEGAN, Susan [B.Sc., Ph.D.]. **Acari as Agents transmitting Typhus in India, Australasia and the Far East.** *British Museum* (*Natural History*). *Economic Ser. No. 16.* 78 pp., 49 figs. (2 maps, 1 folding). 1945. London : Printed by Order of the Trustees of the British Museum. [1*s.* 6*d.*]

The serious military problem presented by scrub typhus in S.E. Asia and the S.W. Pacific during the war was generally quite unexpected. Few people had any practical experience of the disease and a great demand for information and literature therefore arose. Dr. Susan Finnigan's book is intended to make modern knowledge about the vectors of scrub typhus, and of other rickettsial diseases transmitted by mites and ticks, easily accessible to workers in the

field. This sort of information is otherwise almost entirely inaccessible to such workers, and the book should be widely welcomed. Clear diagrams and useful keys make identification of the important species possible.

From the strictly entomological point of view the greater part of the contents of this book will probably require little in the way of fundamental modification in the near future, though additional sections may be required. But since it went to press there have been many papers dealing with the transmission and ecology of the diseases concerned, which will necessitate considerable modifications in future editions. The end of the war will also permit the inclusion of control measures hitherto kept secret.

A most unfortunate misprint occurs in the table giving the characteristics of the rickettsial diseases ; scrub typhus is shown as giving a negative reaction with *Proteus OXK* in the Weil-Felix test. *Kenneth Mellanby.*

Bablet, J. **La fièvre jaune. Diagnostic différentiel clinique et histopathologique. Hépatite amarile.** [Yellow Fever. Differential Clinical and Histopathological Diagnosis. Yellow Fever Hepatitis.] Collection de l'Institut Pasteur. 69 pp., 10 text figs. & 6 figs. (4 coloured) on 3 pls. 1945. Paris : Les Éditions Médicales Flammarion.

The title of this work—" Yellow Fever "—is somewhat misleading, for the greater part, and indeed the only section of any value, is devoted to a reproduction of the author's observations on the histopathology of the disease [see this *Bulletin*, 1936, v. 33, 333, *et seq.*].

After an introduction stressing the importance of viscerotomy for the examination of the liver in all doubtful cases the author gives a brief summary of the principal endemic centres of the disease at the present time. The view is expressed that yellow fever was introduced from the Antilles and America into South America and West Africa. No evidence is adduced in support of this opinion, which is opposed to the generally accepted view that yellow fever was introduced into the Western Hemisphere from West Africa. The account of the symptomatology contains descriptions of a few fatal cases of yellow fever to illustrate what is stated to be a typical form of the disease among Europeans during epidemics, also two atypical examples in which the diagnosis was established by histological examination of the liver. There are also brief chapters on clinical differential diagnosis, and on the various biological examinations which can be used in establishing the nature of the disease.

The main part of the memoir starts with a historical summary of work on the pathological anatomy of yellow fever. Since 1935 the author has been in charge of the histological examination of the livers of all cases of suspected yellow fever from the French Colonies, including the Antilles and Guiana, in addition to West and Equatorial Africa. As a result of the study of hundreds of cases, he has come to the opinion that the histological changes in the liver furnish the best practical method of diagnosis. Two degenerative processes are constantly in evidence, fatty degeneration and necrosis of the hepatic cells. Details are given of the best staining methods, and the changes are illustrated by an excellent coloured plate.

The differential diagnosis of the conditions producing liver changes that might be compared with those accompanying yellow fever are then described and illustrated. The most important are the intoxication effects of carbon tetrachloride, arsenicals, chronic hepatitis, spirochaetal jaundice, etc. An appendix, by Françoise Bloch and M. R. Godin, contains technical details of the methods used for staining paraffin sections of the liver, for the his ological diagnosis of yellow fever. The bibliography includes for the most part only publications dealing with the pathology of the disease.

This memoir contributes nothing new to our knowledge of yellow fever, and its only value lies in the section on the pathological histology of the liver, with its excellent illustrations. *E. Hindle.*

POLAK, Marius Frans. **Vraagstukken der gele koorts. Epidemiologie en vaccinatie.** [Problems of Yellow Fever. Epidemiology and Vaccination.] [Thesis for Doctorate of Medicine, Univ., Amsterdam, 15 Aug., 1945.] 193 pp., 2 figs. (1 map) & 3 charts. [432 refs.] English summary pp. 160–63. 1944. Amsterdam: N.V. Noord-Hollandsche Uitgevers Maatschappij.

The author of this thesis has made an extended summary of the literature on the subject, as his list of 432 references indicates. The book was written in Holland, however, and few of the papers quoted are dated later than 1940, so that full information was not available to the author on the wartime experience of vaccination in American and British troops, and on the epidemic in the Sudan which began late in 1940, and of which only the beginning is here referred to.

The chapters contain information on :—Recently acquired knowledge of the epidemiology of yellow fever ; an investigation into its spread in Surinam ; the modifications in the virus produced by passage in animals ; vaccination with attenuated virus ; vaccination experiments carried out in Amsterdam with virus 17D ; and a comparison between the methods of vaccination with the French neurotropic strain and the American 17D.

Protection tests in Surinam indicate that jungle yellow fever exists there, that in the Negroes the men run greater risk of infection than the women, probably because their work takes them more closely into contact with the forest, and that in the aboriginal Indians the risks to the sexes are about equal.

Charles Wilcocks.

VANNI, Vittorio [Direttore inc. dell'Istituto di Parassitologie del'Università de Roma]. **Terapia clinica delle malattie da zoo-parassiti dell'uomo.** [Clinical Therapy in the Parasitic Diseases of Man.] Prefazione del Prof. Vittorio PUNTONI. 256 pp., 37 figs. 1944. Rome: Editrice Nazionale. [L. 335.]

In the first part of this book the author discusses the general principles of chemotherapy and describes the chemistry and therapeutic action of arsenicals, antimonials, acridine derivatives and other drugs which have a bearing on the treatment of protozoal infections. In a similar section he deals, more briefly, with anthelmintics, but gives in considerable detail the procedures he advises in the preparation of the patient and the administration of the drugs. In this section male fern, santonin, chenopodium, carbon tetrachloride and other compounds are described.

The second part of the book is devoted to the various diseases in relation to the treatments available, and contains some brief notes on diagnosis. The protozoal diseases include those due to intestinal protozoa and to the blood and tissue parasites. American trypanosomiasis is not included. The helminthic diseases include all the common conditions. In a final section are considered myiasis, scabies and pediculosis.

This book was published early in 1944, and was, no doubt, written before the liberation of Italy. The author was not, therefore, able to consult the most recent work done on some of these subjects by the members of the British and American forces. Nevertheless, one would have expected some reference to the aromatic diamidines in leishmaniasis and trypanosomiasis, and a more favourable account of tetrachlorethylene in hookworm infestation. On the whole,

however, this is a careful collection of information on most of the known treatments for the conditions with which it deals, but it will need considerable modification and amplification, in the next edition, when the author has had opportunity to assimilate all the work which has recently been done.

Charles Wilcocks.

Julião, Oswaldo Freitas. **Contribuição para o estudo do diagnóstico clínico da lepra nervosa.** [A Study of Nervous Leprosy and its Clinical Diagnosis.] [Thesis, Fac. of Med., Univ. S. Paulo, 15-1-1945.] 203 pp., 84 figs. on 28 pls. & 12 text figs. 1945. São Paulo: Industria Grafica José Magalhães Ltda.

A literal translation of the title of this book would fail to convey the extent of the information which it contains. The author has had unique opportunities for observing and studying nervous diseases in general and the nervous lesions of leprosy in particular, and he has made the most of these opportunities with the result that he has produced a book which must surely prove to be the last word in " nervous leprosy " for a long time. It is not a book to be read through or continuously, but all practising leprologists should have a copy for ready reference.

The importance, the difficulties, and the responsibility of making a diagnosis of " nervous leprosy " are very great. The veriest tyro cannot fail to diagnose leprosy in its developed stages with disfigurements, deformities and mutilations, or even earlier in the tuberose form ; it is in the early stages, and above all in the early nerve-stages, that difficulties arise, and they may be great.

No one could be better qualified than the author to pronounce *ex cathedra* on this question. He possesses for his task the dual qualification of being neurologist to the Department of Leprosy Prophylaxis in São Paulo and at the same time a member of the staff of clinical neurologists of the Faculty of Medicine of the São Paulo University.

The author, therefore, has abundant material at his disposal and, for purposes of description, he has divided the work into three sections, or chapters, but from the nature of the subject these must to some extent overlap. At the same time, unless some such subdivision were made, it would be difficult to avoid confusion. The first chapter is named the *Nervous Manifestations of Leprosy* and treats in detail, with exemplary cases to illustrate them, of definite or more or less isolated clinical symptoms such as conditions affecting motility of digits or of larger muscular associations of the limbs, affections of the cranial nerves, changes in the reflexes, superficial and deep, of the cutaneous vasomotor system, of sweating and of sensory and trophic disturbances—cutaneous atrophy, ichthyosis, sclerodermia, " glossy skin," alopecia, onychia, perforating ulcer of the sole, bone resorption, etc.

The second chapter is the shortest of the three, occupying 30 pages, or one-fourth the length of the first. This chapter is concerned with the *Clinical Forms of Nervous Leprosy* and is itself divided to describe three groups of cases : the first according to the localization of lesions, neuritis, monoplegic, paraplegic, hemiplegic ; the second according to the predominance of one or other classes or association of symptoms—sensory, motor, trophic, psychic or mixed ; thirdly, according to the course, whether acute, subacute or chronic and benign, stationary or retrogressing. This chapter ends with an account of diagnosis of nervous leprosy by means of biopsy specimens of the suspected nerve. Examination of these rarely reveals bacteria, but the histological changes are fairly distinctive and characteristic—attenuation of the myelin sheaths and Wallerian degeneration. This method is of particular importance

because in many of these cases the routine tests, serological, immuno-biological and bacterial examination of the nasal mucosa, give no positive information.

Chapter III, though only 50 pages are given to it, is of great clinical diagnostic interest. It deals with the differential diagnosis from non-leprotic nervous diseases: lesions of the neuraxons—syringomyelia, intramedullary tumours and haematomyelia; from amyotrophic syndromes—amyotrophic lateral sclerosis, syphilitic spinal amyotrophy, the Aran-Duchenne type, and tabes. Secondly, from affections of the nerve roots and plexuses—herpes zoster, cervical hypertrophic pachymeningitis, chronic meningo-radiculitis. Next, from peripheral nerve affections—polyneuritis, neuromata, the Charcot-Marie-Tooth type of progressive amyotrophy and von Recklinghausen's disease.

Diagnosis from conditions resembling leprosy in certain features, though not of nervous origin, is not omitted; among them sclerodermia, ainhum, Dupuytren's contraction, endarteritis obliterans and its effects in causing ulceration and gangrene, and functional, hysterical, anaesthesia.

In almost every instance one or more case-histories illustrating the point under discussion are presented. In conclusion, this book may be unreservedly recommended for the use of all engaged in the work of diagnosing and treating lepers, or interested in the subject of leprosy. The letterpress is neither too compressed nor prolix, and is interestingly written. The illustrative cases have been carefully selected and the illustrations themselves, photographs, photomicrographs and line drawings, have been excellently reproduced.

H. Harold Scott.

Possolo, Helena. [Quimico-Farmacêutica do Departamento de Profilaxia da Lepra, da Secretaria da Educação e Saúde Pública.] **As flacourtiáceas antilepróticas.** [Members of the Flacourtiaceae employed in Leprosy.] Monografía do Laboratorio Quimico-Farmacêutico do Instituto "Conde de Lara." Trabalho laureado com o prêmio S. Lucas 1940 pela Academia Nacional de Medicina. 132 pp., 95 figs. 1945. São Paulo: Diretoria de Publicidade Agrícola.

To this work was awarded the São Lucas Prize for 1940, by the National Academy of Medicine, São Paulo. The author is the Pharmaceutical Chemist to the Department of the Public Health Service concerned with the Prevention of Leprosy.

The book opens with a brief historical sketch of the use of the oils of the Family of plants, grouped under the name Flacourtiaceae, which have been tried in the treatment of leprosy and includes a map on a very small scale indicating the world incidence of the disease. This introduction is too sketchy to have much informative value. Next follow chapters on various members of the Flacourtiaceae, first of the Oncobeae with descriptions of the various species, their local names, habitats, the chemical composition of the several oils, with keys to the Genera *Lindackeria*, *Mayna*, and *Carpetroche*. Many of the plants, fruits, seeds and leaves are depicted. From the point of view of description of plants, Chapters II and III are the most important in the book. The former contains a key to the chief sub-genera, *Euhydnocarpus*, *Taraktogenus* and *Asteriastigma*; the latter a botanical study which comprises the local names, the habitats, the botanical distribution, the morphology of the fruits and seeds and the chemical composition of the oil of over 50 species and subspecies of *Hydnocarpus*. The fourth and final chapter deals with the chemistry of the oils and the technique for estimating the constituents. Appended is a fairly full bibliography for each chapter. The whole should prove valuable as a work of reference and a copy should be made available in Colonial Chemical and Agricultural libraries. No information is given regarding the clinical use

of any of the substances mentioned, consequently the book makes no appeal to the medical practitioner in the tropics. The illustrations, 95 in number, are clear and well reproduced. *H. Harold Scott.*

SWELLENGREBEL, N. H. [Professor of Parasitology, University of Amsterdam] in collaboration with E. VAN DER KUYP [Government Physician, Paramaribo]. **Health of White Settlers in Surinam.** *Colonial Institute at Amsterdam. Special Publication No. 53. Dept. of Tropical Hygiene No. 16.* 1940. pp. vii+118, 5 diagrams & 3 maps.

This publication is dated 1940 and has only recently reached this Bureau, but it contains so much important information that it is necessary to draw attention to it even at this late date. It is the outcome of the work of a Commission appointed in 1938 by the International Refugee Colonization Society (the Hague) to study the question whether Dutch Guiana could be regarded as a suitable country in which Jewish refugees from Europe could settle. The Commission consisted of the author, an agriculturist and an agricultural economist ; its work in Surinam (Dutch Guiana) occupied several months, and its members made careful search of records to supplement their personal findings. The war, however, frustrated the project of a joint report, but it was considered advisable to publish in English the results of Swellengrebel's investigation.

The first part deals briefly with general information on the colony, and with the health conditions as they have recently existed. The chief points are that the recorded death rates in rural areas are remarkably low, and that those recorded in the town of Paramaribo do not indicate that tropical diseases are very prevalent. There is a discrepancy in that malaria is more common in the rural areas than in the urban, and that this is not reflected in the known death rates.

In Chapter III is given the sanitary history of white settlement in Surinam. Portuguese Jews were settled there by 1694, but this colony did not finally prosper ; health records of this community do not exist. In 1845 immigrants from Holland settled at Kwatta, and after two disastrous epidemics, one in 1845 due probably to typhoid, and one in 1851 due to yellow fever, these people prospered. Other settlements in various parts of the country are referred to, and the general conclusion from this actual experience is that white settlement is possible and that immigrants who choose their ground with care in relation to malaria, and who live in accordance with reasonable standards in relation to water supply, disposal of excreta, consumption of a good diet (which is quite possible with the local foodstuffs), and malaria need have little fear of their health. Malaria is, indeed, prevalent in the rural parts of Surinam, where *Anopheles darlingi* (the most dangerous vector) exists, but there is little on the coast where *A. tarsimaculatus* [? *A. aquasalis*] is the not very effective vector. *Plasmodium falciparum* is found, especially in the *A. darlingi* areas, and the Bush Negroes and Indians are the reservoirs of infection. Coastal malaria in Surinam " is of much less importance than in many other countries of the wet tropics. That fact strongly supports Surinam's claim to becoming the permanent home of European colonists." But malaria should not, nevertheless, be underrated.

The other diseases which need consideration in respect of European settlement are the excremental diseases—hookworm, schistosomiasis, enteric fever and the dysenteries—together with filariasis, yellow fever (absent since 1909), yaws, leprosy, trachoma and affections of the kidneys. All can be kept down

or avoided in any settlement in which the known appropriate preventative measures are applied.

The conclusion to which Swellengrebel's work leads is that if there is any argument valid against the introduction of Jewish refugees as settlers in Surinam, it is not the argument of undue danger to their health. The climatic conditions *per se* do not contraindicate white settlement, and the incidence of disease, for a tropical country, is low. The point is made, however, that small communities lead to inbreeding, and that attention should be given to this fact.

Readers of this volume will find in it much that may have a bearing on similar problems elsewhere, though many of the conditions in Surinam are not common elsewhere in the tropics. *Charles Wilcocks.*

Bobrinskoy, N., Kuznetzov, B. & Kuzyakin, A. [**Mammals of USSR.**] 440 pp., 256 figs., 32 pls. & 62 maps. 1944. Moscow: Issued by Government Publishing Office "Sovietskaya Nauka." [In Russian with an English Preface.]

This is a useful reference book, compiled "to aid any person somewhat familiar with the subject to determine the specific name of any of our mammals, and to receive a more or less complete information on the geographical distribution of the mammal on the territory of this country," though the information concerning the more remote areas is as yet incomplete.

Keys are given, and for each species there are notes on morphology and biology. The geographical distribution is summarized in 62 maps at the end of the volume. There are many line drawings of skull and tooth structure, and 32 half-tone plates of most attractive pastel and wash drawings (in monochrome) of the animals in their natural surroundings.

To the epidemiologist the long section on the Rodentia will be of most value. *Charles Wilcocks.*

League of Nations. **Report on the Work of the League during the War, submitted to the Assembly by the Acting Secretary-General.** Ser. L.o.N.P. General. 1945. 2. 167 pp. Geneva. 1945, Oct. [Allen & Unwin Ltd., 40 Museum Street, London, W.C.1.] [2s.] [Review appears also in *Bulletin of Hygiene.*]

The old League of Nations will shortly by replaced by the new United Nations Organisation and the terms of transfer are now under discussion. This report by the Acting Secretary-General, prepared for submission to the League of Nations Assembly which will be convened in 1946, presumably for the last time, describes the work done by the various League Committees and by the Secretariat since 1940, and shows how League organs have adapted themselves to war conditions, and how, in spite of the breakdown of the political system of the Covenant, the non-political technical services have not only survived, but have been performing vital and most valuable duties throughout the war period.

The introductory pages refer to the potential usefulness of the League's activities as a basis for post-war reconstruction and to the problems connected with their transfer to the new United Nations Organisation. An assessment of the value of the League's first "great experiment" in world organization is also attempted.

Chapter 1 of the report deals with the work of the Economic, Financial and Transit Department of the League—made easier by the transfer in 1940 of a part of its staff to the United States, where a base was set up for observation and intensive research on questions relating to the reconstruction of the world's economic life after the war.

The social and humanitarian activities of the League are then reviewed in Chapter 2, and here an account is given of the work of the Health Organisation which, with a staff reduced by 1940 to two doctors—the Officer in charge of the Health Section and the Chief of the Epidemiological Intelligence Service—remained in Geneva to perform the heavy task of preserving what could be preserved of the work of the past, and of adapting the efforts of the Health Organisation to the new conditions resulting from the hostilities. In the early years of the war national health services were helped both by direct action and by the supply of documentation and technical advice, and reports were prepared for their guidance on such subjects as the medico-social problems arising from the displacement of civil populations. Data were also supplied on a variety of matters, including the food ration consumed before and during the war in the occupied countries, the foodstuffs most suitable for distribution in concentrated form to the populations of these countries after their liberation, and the types of vitamin deficiency disease that were most to be feared.

Later, in 1943, the Officer in charge of the Health Service of the League was sent first to London to place at the disposal of the Inter-Allied Services the experience acquired by the Health Organisation in connexion with the combating of epidemics, the prophylaxis of contagious diseases, and assistance for pregnant women and newborn infants, and then to Washington to give to the Office of Foreign Relief and Rehabilitation the benefit of the League's nutritional, malarial and sanitary engineering experience, and to develop collaboration between the League Health Organisation and the Health Division of UNRRA which was in process of organization. Arising from this, the League's Health Section established a "research unit" in Washington in 1944—staffed by its former Chief of the Epidemiological Intelligence Service at Geneva and by the former statistician of the League's Singapore Bureau—which has since become the Epidemiological Intelligence Service of the Health Division of UNRRA.

Meanwhile many of the pre-war long-term activities of the League Health Organisation continued, including the work on biological standardization, on the unification of the national pharmacopoeias, and on malaria, rabies and nutrition.

After this account of the work of the Health Organisation, the remainder of Chapter 2 is devoted to the League's work on the control of the drug traffic, international assistance to refugees, the settlement of the Assyrians of Irak, and technical collaboration with China.

The remaining chapters deal with Mandates, Intellectual Co-operation, Questions of a Legal and Administrative Character, and the Library at Geneva. The report ends with a list of the League of Nations Publications from January 1st, 1940, to October 31st, 1945.

This account of the first great experience in international co-operation for peace and human progress goes far to show that "the League did not fail; it was the nations which failed to use it." If the lesson is learned that, however effective the machine may be, the outcome "will depend on how it is used, on the justice, wisdom and courage of leaders, and above all, on the vision and determination of the common people," it will have contributed much to the success of the new venture on which the United Nations are now embarking.

R. L. Sheppard.

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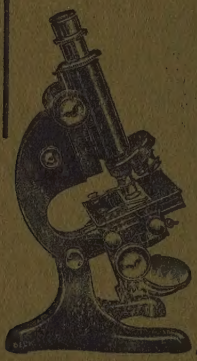

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